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FIG. 1



FIG. 2



FIG. 3

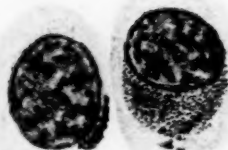


FIG. 4

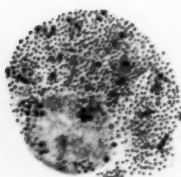


FIG. 5

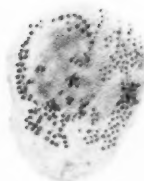


FIG. 6

FIG. 1 (THYGESON). EARLY INITIAL-BODY INCLUSION SHOWING BEGINNING DIVISION OF INITIAL BODIES.

FIG. 2 (THYGESON). INTERMEDIATE INCLUSION.

FIG. 3 (THYGESON). INTERMEDIATE INCLUSION.

FIG. 4 (THYGESON). ELEMENTARY-BODY INCLUSION, LEFT, INITIAL-BODY INCLUSION, RIGHT, ILLUSTRATING COLOR DIFFERENCES.

FIG. 5 (THYGESON). LARGE ELEMENTARY-BODY INCLUSION. A FEW INITIAL BODIES REMAIN. NUCLEUS UNDERGOING DEGENERATION.

FIG. 6 (THYGESON). ELEMENTARY-BODY INCLUSION. NUCLEUS UNDERGOING DEGENERATION.



## A FUNCTIONAL STUDY OF THE NERVE ELEMENTS OF THE OPTIC PATHWAY BY MEANS OF THE RECORDED ACTION CURRENTS

GEORGE H. BISHOP, PH.D. AND S. HOWARD BARTLEY, PH.D.  
SAINT LOUIS

Records have been made of the small output of electricity that is the result of the activity of a nervous element; they form an index of such nervous activity, being subject to analysis as to the response of distinct groups of fibers in the nerve. The optic tract responds to stimulation of the retina by a beam of light in characteristic fashion. The response of the optic nerve is by a series of impulses relative to the intensity and duration of the beam, after a latent period. The summation of these impulses in the thalamus sets off an impulse to the cortex, again after a latent period. The cortex gives at least two types of electrical response. Any one pathway seems to be conducting only part of the time, due to the independently rhythmic activity of the thalamus, which is therefore periodically nonirritable to optic-nerve impulses. The optic cortex, also independently rhythmically active, responds characteristically to optic-nerve stimulation.

In the authors' opinion, the act of seeing is a disturbance of the individual pattern of visual-cortex activity, rather than the superimposition of a new activity of different type upon it.

From the Laboratory of Neurophysiology, Oscar Johnson Institute, Washington University. Read before the Association for Research in Ophthalmology, in Cleveland, June 12, 1934.

The ophthalmologist is naturally tempted to think of the eye in terms of its defects, since these are called to his notice for correction. A pathological condition, however, is only recognized in terms of its deviation from the normal. The study of normal function is most urgently needed in regions where least is known, and this is perhaps a sufficient justification for bringing to the attention of ophthalmologists the results of certain studies on the normal functioning of the nervous mechanism of vision. Even though, at present, the information derived from experiments on normal nervous function may not be directly applicable to clinical purposes, the first step must be to obtain the information that might eventually become applicable when enough is known.

The question then arises, what sort of information can be obtained by the technical procedures employed in studying nerve structures generally, on the functioning of so complicated a structure as the visual apparatus? First, it is known that nerve tissue, in general, including the retina, gives off electricity when active; we can therefore record these electrical "action currents" as

signs of this activity in unconscious or at least noncommunicating animals, after taking suitable steps to expose the structures concerned. Second, we can perform experiments, less comprehensive, perhaps, but on a conscious human subject whose description of the result in sensation will allow us to infer the relations of the action currents we record, even in animals, to sensation. Third, we can correlate the electrical responses from different structures with the analyses which anatomists have made of their functional relations. Fourth, and by no means least, we can observe the time relation of responses in various nerve elements, and the effects of various types and sequences of stimulation, and correlate the results with what we know about the visual process from other sources. For instance, phenomena of flicker and flicker-fusion have been elaborately studied in man. We may, by observing the electrical responses of the optic nerve, or of the optic cortex, to repeated stimuli of various frequencies, obtain the physiological picture that corresponds to flicker phenomena in sensation.

The first step is to expose the nerv-

ous elements in animals and to record the effects of their activation, under as simple and as well-controlled conditions as possible; and certain results obtained in this manner will be presented below. The nerve mechanisms concerned consist of the retina, optic nerve, thalamus, and cortex, and their interconnections, and we have found rabbits suitable animals in which to study these structures. However, many other nervous mechanisms are involved in the act of seeing besides this direct pathway from the rods and cones to

pulses, sensory impulses from endings in the eye other than in the retina, such as muscle-sense endings, assist in interpretation of the visual image. Thus the main optic pathway is only a small part of the nervous mechanism of vision, as the telescope which transmits light from the stars is a small part of the machinery that controls and operates it. What follows, however, is concerned with the optic pathway proper, analyzing the visual impulse started by light falling on the retina as it passes over various parts of the nervous pathway to the cortex.

When light falls upon the rods and cones, nerve fibers are secondarily stimulated, that is, the energy of the stimulus changes from light or wave energy, first to chemical energy (in the breakdown of visual purple for instance) and then to nervous energy, again chemical or physico-chemical. From here on, the chain of events set up may be termed the *visual impulse*, as contrasted to the visual stimulus of light. This visual impulse is made up of many nerve impulses, one nerve impulse, or one series of them, in each fiber activated. If all, or a number of fibers are activated at the same time, we may speak of a volley of impulses. If the nerve impulses are not synchronized, it will be a random discharge. Each nerve impulse passing from the sense cell must "change cars" at each synapse between nerve cells, and then it proceeds over the next fiber. Synapses occur in the ganglion-cell layer of the retina, in the thalamus, and in the cortex, and in these regions there is evidence that the nerve impulse in one fiber may affect the activity of parallel fibers. Between these "exchange stations" the impulses are independent of each other.

If we think then of parallel pathways from retina to brain (fig. 1) with three regions of possible cross-connection, we may inquire what the character of the visual impulse is at any level. It can be described in simplest terms where it passes over nerve fibers. At the levels where the visual impulse is traversing nerve fibers, it consists entirely of nerve impulses. In the rods and

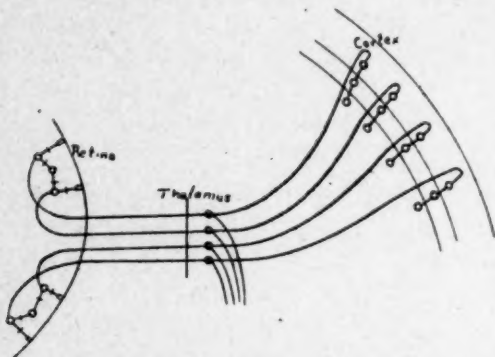


Fig. 1 (Bishop and Bartley). Diagram of parallel paths from eye to brain. Circles represent nerve cells, lines connecting them represent nerve fibers, lines across the latter represent synapses, at which regions the impulses in one fiber path may affect the passage of impulses over other paths.

the brain. We might differentiate between this main nerve pathway for vision and the nervous activity of other parts which secondarily affects the efficiency of the visual act. Whatever the activity of the retina at a given instant, this activity will be altered if the subject turns his head, by means of nerve impulses sent to the muscles of his neck. If other impulses over the oculomotor nerve reach the recti muscles, the eye will be turned, again altering the field of vision and changing the retinal activity. Dilatation or constriction of the pupil, activity of the ciliary muscles, or lids, vasomotor changes in the retina, all are brought about by nerve impulses secondary to visual impulses, but still assisting in determining what visual impulses the brain receives. Besides these motor im-

cones, it consists of a chemical change. At the levels of cells and synapses, it consists of cell impulses which differ from nerve-fiber impulses. If one could count each nerve impulse in each fiber of the optic nerve, assigning each impulse to its proper fiber, he would have a complete description of the visual impulse at the optic-nerve level. To describe the whole visual act, however, he would have to know this for each level of the visual pathway, including the cortex. He would have to know which fibers and cells were active, and whether that activity consisted of one impulse, or of how many, and at what speed each conducted, and how frequently impulses followed each other in each fiber, and particularly how these phenomena changed when the nerve impulses passed across synapses from one set of fibers to another. He would then have only a *physiological* description of the visual act, not a mental one; but he would have more than an anatomical one.

The authors have been attempting to describe the visual impulse in terms of nerve activity. Since the visual apparatus is too complicated to study as a whole, one is tempted to take it apart and observe the pieces separately, like a dismantled clockworks. Instead of starting the visual process by allowing a complex visual pattern to fall on the retina, we employ simpler stimuli, such as short flashes of light, or electrical shocks, which can be accurately controlled. This corresponds to pushing one wheel of the clock at a time to see what it connects with. Since each nerve impulse in each fiber or cell produces a minute quantity of electricity, these impulses can be detected by an electrical recording device. This device consists of a vacuum-tube amplifier and a cathode-ray oscillograph, of such sensitivity that the form of impulses whose electrical output is measured in hundredths of a millivolt and which last less than a thousandth of a second can be accurately photographed (fig. 2). The oscillograph thus records from a given part of the nervous

system a picture that corresponds to the electrocardiogram from the heart, and by taking note of the direction and position of leads, shape and size of electrodes, and anatomical structure of the parts concerned, this record can be interpreted in a manner quite analogous to the interpretation of the electrocardiogram. In what follows, the technical details of this interpretation will be largely omitted, and the result presented as a tentative description of the visual process, not a final explanation.

We may first examine the nerve fibers passing from the retina to the thalamus. For simplicity, an animal is

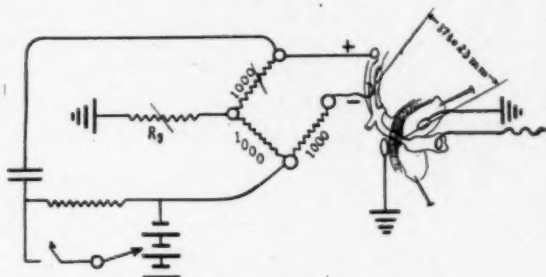


Fig. 2 (Bishop and Bartley). Arrangement for stimulating the optic nerve and leading off its action currents, leaving the blood supply intact. The + electrode of the stimulating apparatus is on the cut brain surface, the — electrode touches the optic nerve above the chiasma. The grounded lead of the recording apparatus rests in the orbit, the other lead, to the grid of the amplifier, is attached to the remnant of the optic cup, the nerve being dissected clean between. Since the nerve dies where clean dissection stops its blood supply, action currents are recorded from the point where it leaves the orbit.

chosen (rabbit or frog) most of whose fibers cross over at the chiasma to the opposite side. Stimulating electrodes are placed on one end of this tract, and recording electrodes on the other, after the minimum of dissection required has been completed. The impulse passes in either direction with equal facility. Through the stimulating electrodes on the nerve a single electrical shock is applied, and is varied in strength with successive trials, until at a specific strength, an electrical nerve response appears at the recording electrodes after a delay due to conduction along the fibers. Above threshold strength of shock, this potential wave increases in



amplitude as more fibers are activated, up to a maximum (fig. 3). At about this strength a second potential wave appears later than the first, from a second group of fibers which require a stronger stimulus to activate them, and which conduct their impulses more slowly. Finally, at a still higher strength of stimulus, a third and still slower potential wave appears, and, after this has reached a maximum, further increase of

in such nerve trunks occur in size groups, with maxima and minima alternating in the number of fibers of different sizes. (3) Each group corresponds to one or a few functions served by a nerve; i.e., touch in skin nerves is found in one group, pain in another, and sympathetic fibers to blood vessels in a third. In the cervical sympathetic trunk, one group of fibers activates the pupil of the eye, another

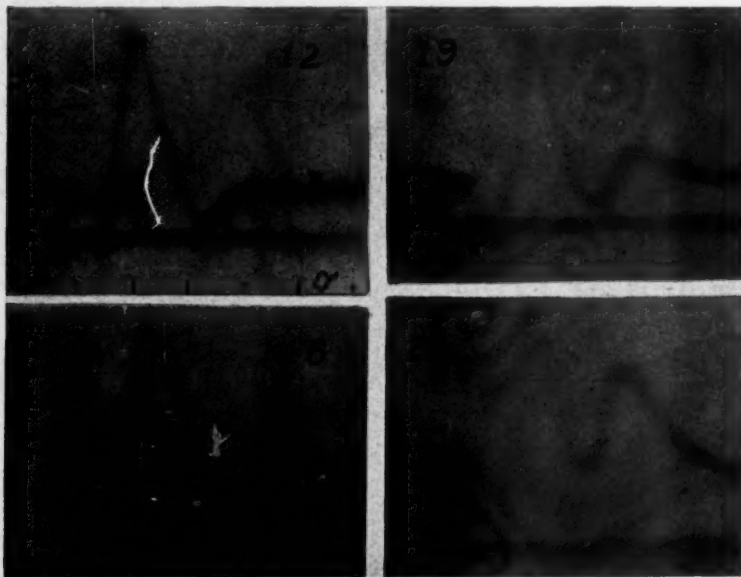


Fig. 3 (Bishop and Bartley). Optic-nerve records of potentials. Taken from a series of 22 records, following increasing strengths of stimulation. Records 12 and 16 show only one potential wave, indicating one group of fibers of relatively low threshold, while in record 19 a second wave is appearing, due to a second group of nerve fibers, and in 21 the second wave is maximal.

the stimulus does nothing; all the fibers of the optic nerve have been activated.

Many other nerves have been investigated by this technic, and the picture resulting from stimulation has been compared with the histological content of fibers in each nerve. The following relationships have thus been established: (1) The larger the diameter of a nerve fiber, the faster it conducts its impulse, and the easier it is to stimulate electrically. (2) In practically all the nerves investigated, the action potentials are not simple, but occur as a succession of more or less discrete waves. This means that the nerve fibers

group constricts blood vessels, and a third group is sensory. (4) By differences in various properties as measured from their action potentials, sympathetic or parasympathetic fibers, i.e., motor fibers innervating the viscera, can be differentiated from somatic fibers, motor and sensory. By analogy then with other nerves, one should expect to find mediated in the optic nerve three functions, and of these, the first two, corresponding to the first two potential waves, should be two sensory aspects of vision, and the third a motor visceral function possibly affecting the health or the receptivity of the retina,

or maintaining it in a suitable condition to receive and transmit to the nerve fibers visual stimuli. These functions have not been positively identified, but some further evidence exists for their being distinct from one another.

Examination of the optic-nerve cross section shows fibers with a wide range of size. These fibers are thoroughly scattered, however; there is no one region containing all the large fibers, for instance, but these are distributed throughout the nerve. This has significance in two respects: first, since it is known that the spatial arrangement of fibers in the optic nerve corresponds to the arrangement of their endings in the retina, and since different conduction rates indicate different fiber sizes, we can infer that the two size groups of fibers indicated by the two potential waves both serve visual functions represented in all parts of the retina (in the rabbit). Secondly, an electrical shock applied to the nerve selectively activates fibers from all parts of the retina according to their size.

This means that an electrical stimulus applied to the optic nerve (left with its central connections, but with the eye and retina cut away), strong enough to call forth the first potential of this nerve, acts analogously to a short flash of light that illuminates the whole retina. It is even simpler than this, for while the shortest flash of light probably sends several successive impulses over each optic-nerve fiber activated, an electrical shock sends only one impulse over each fiber. An increase in intensity of the light will increase the number of sense cells activated, since some have higher thresholds than others; it will also increase the number of impulses sent over each fiber, since the greater the stimulus to a given sense organ, the more frequently it fires off to the nerve. An increase in the strength of the electrical stimulus will similarly activate more fibers, since here again there are differences of threshold, but in this case, the number of impulses per fiber is not increased. Stimulating the nerve directly, therefore, enables us to alter only one thing at a time; increasing stimulus strength increases the number of fibers

acting, and repeating the stimulus at any frequency desired, we may imitate, under controlled conditions, the action of the retina on the optic-nerve fibers.

With the end of the optic nerve exposed in the eye socket, we may stimulate the stump, and by means of electrodes placed in the optic cortex, find what character of impulse arrives at the brain. When a single volley is sent up in only a few nerve fibers (from a single shock near threshold), the impulse does not reach the cortex with enough energy to be detectable. This may be because we cannot yet detect a small cortical impulse. We have reason to believe, however, that the impulse does not get through to the cortex unless either a considerable number of fibers are activated, or else fewer fibers are activated repeatedly. Increasing the strength of single shocks to the nerve finally results in a cortical response; but here a new complication enters. If a relatively weak shock is repeated once a second, for instance, some responses will follow the shocks, but not every shock will be effective. Since we know by direct observation that each shock activates the nerve, we infer that somewhere below the cortical level, probably in the thalamus, a variation in sensitivity is taking place, quite independently of our stimulation. If now we increase the strength of the stimulus, activating more nerve fibers, a strength is reached such that every stimulus is effective at the cortical level, but not all are equally effective. A large response may alternate with a small one, or successive responses may fluctuate rhythmically up and down. Again, since we know that the optic nerve responses are not varying in any such manner, we infer a rhythmical alteration of excitability in the subcortical levels of the pathway, probably in the thalamus. Finally, if the optic-nerve stimulus is still further increased, activating still more fibers, each response from the cortex is fully developed; that is, all are of the same size. This rhythmical loss of excitability can be overcome if enough fibers are stimulated (fig. 4).

With a stimulus below maximal, and a response that is therefore fluctuating

rhythmically, it is possible to investigate the character of this rhythm. If even weak stimuli are applied more frequently than once per second, a frequency may be found that produces a series of responses all of which are of the same size. A slight change, either increase or decrease of rate, restores the fluctuation. Obviously we are dealing here with a natural periodicity of the nervous mechanism. The nerve cells

It may be argued that such a fluctuation in response does not correspond to visual fact; that we do not see by fraction-of-a-second intervals but continually; and that the results of electrical stimulation of the optic nerve are hardly comparable to visual processes in the intact animal. It is, however, possible to record from the cortex the responses to the more complicated stimuli of light flashes in the intact eye. Under

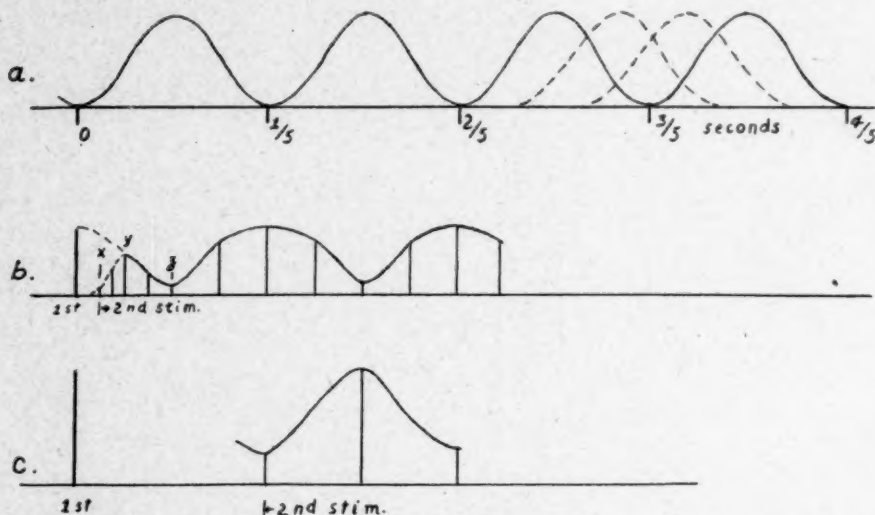


Fig. 4 (Bishop and Bartley). Diagram to indicate a rhythmic variation of excitability of the optic pathway. The continuous curve in *a* represents the excitability of one fiber pathway or group of pathways, whose excitability varies from minimal to maximal at  $1/5$ -second intervals. The dotted curves represent other pathways varying similarly, but out of phase with the first, so that at any instant some pathway will be excitable, permitting continuous vision in spite of discontinuous functioning of any one pathway. The second line, *b*, indicates the size of the response obtained from the second stimulus to the optic nerve, when a first stimulus precedes it. The first stimulus makes the pathway refractory, after which its ability to respond varies rhythmically. The third line, *c*, shows a similar effect for shocks of different intensity.

themselves are varying in sensitivity, and only if each of a succession of stimuli falls in a sensitive phase of the nervous rhythm, will each cause a cortical response. If each falls in an insensitive phase, no responses will occur. If the two cycles, of stimulation and of natural responsiveness, are exactly in time, all responses are alike, but if slightly out of time, fluctuation occurs in amplitude of the response. The critical frequency, that is, the frequency at which any given nerve cell becomes sensitive, is about five per second.

these circumstances also, a similar fluctuation occurs as a result of repeated identical stimuli, when the latter are relatively weak. The phenomenon is therefore quite physiological. Consideration of the character of the cortical response in general may give further evidence as to its meaning.

The optic as well as other regions of the cortex show continual electrical activity, quite independent of specific stimulation from the periphery (figs. 5, 6). These "spontaneous" responses appear as an irregularly varying series of



waves, the largest of which may be as much as  $1/2$  millivolt in amplitude, such waves varying in duration from 20 to 50 or more thousandths of a second. Responses to specific optic-nerve stimuli may be of much higher voltage than this, and can therefore be recorded as peaks emerging from the lower successions of waves, although near the

of about four per second. Stimulated directly by electrical shocks, between responses, it can be made to respond out of phase, like an extra systole in the heart. When such a region is normally in place in the cortex, different groups of cells in the region are apparently connected by different pathways to other regions, from which they ob-

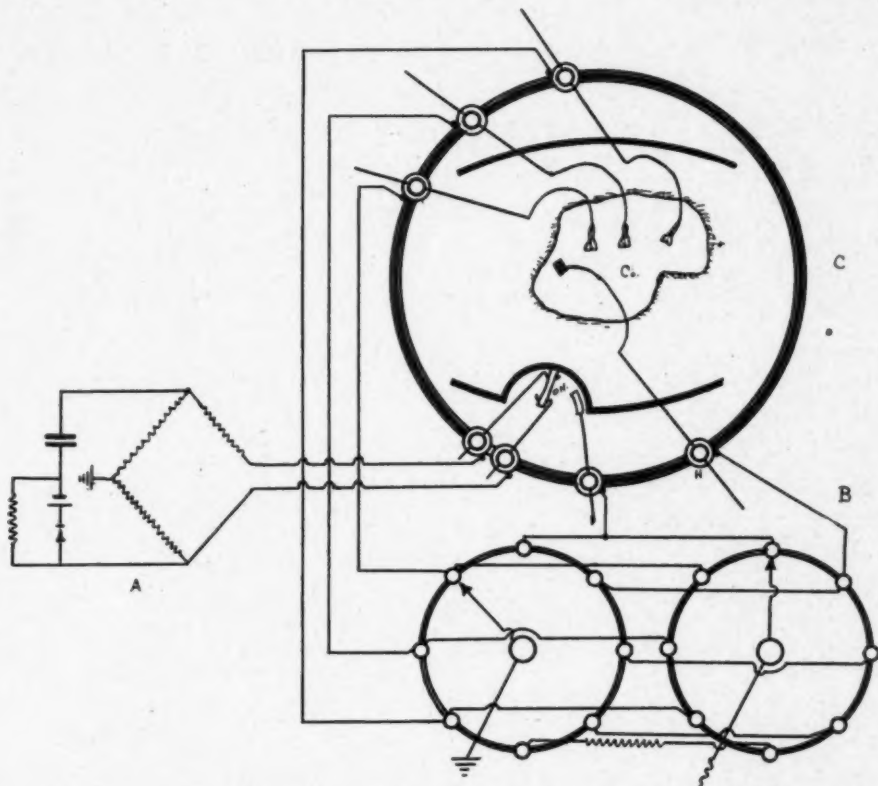


Fig. 5 (Bishop and Bartley). Diagram of apparatus for stimulating the optic nerve and leading the resultant action currents from the optic cortex. Different electrodes on the cortical surface can be connected to either recording lead to the apparatus by the switches below.

threshold of stimulation it is more difficult to recognize them. This continuous activity, although irregular, is presumably made up of regularly rhythmic oscillations, out of phase with one another. This can be shown by separating a flap of cortex by knife cuts, leaving a hinge attachment to the brain. When such a flap receives via its "hinge" both a blood supply and the necessary nervous connections, it can be observed to respond with a simple regular rhythm

tain stimuli, and since such stimuli are not all in phase with each other, different groups of cells respond at different times, with resultant confusion in the record which represents all of them. The spontaneous activity may thus be no more complicated essentially than the response to stimulation.

It thus appears that different cells in the cortex are active at different times, so that at any instant *some* cells are active. In general, it is difficult to stimu-

late a nerve structure that is already responding, we say that it is partially or wholly "refractory." When a given group of cells is active they will be hard to stimulate, or will give a small further response if stimulated, while groups of cells that are momentarily

Continuous vision might thus be explained as taking place by means of nerve cells which are only periodically active; that is, the cells function successively, one cell relieving another.

However, this has a further bearing on the organization of the visual mech-

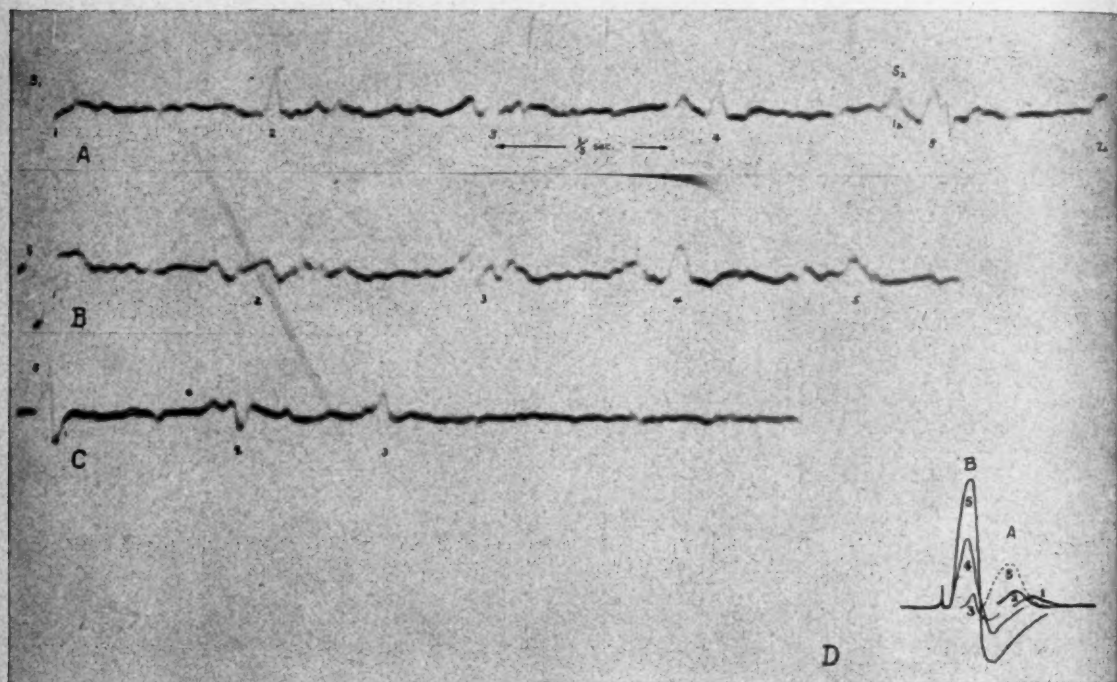


Fig. 6 (Bishop and Bartley). Records from the optic cortex. A, a single shock to the optic nerve at time  $S_1$ , results in 5 successive responses from the optic cortex, marked 1 — 5. At  $S_2$ , a second stimulus was applied to the optic nerve, starting a second series of responses, before the first had ended. B, a series of responses showing variation of form of the individual waves, 1 — 5. Between these, as in the previous record, the irregularity in the base line is due to the spontaneous activity of the cortex, lower in intensity than the waves induced by stimulation of the nerve. C, a series of responses showing only 3 elements, one of which (2) is reversed in direction. The sensitivity of the recording apparatus is cut down so low that the spontaneous activity hardly shows. D, the pictures resulting when a shock to the optic nerve is successively increased from that giving a threshold response. Only the first response of the series of 3 to 5 in previous records is analysed. 1 to 5, results of 5 shocks of increasing strength. The late potential (1) becomes larger and falls earlier (2) until at 3, a second potential rises ahead of it, and in 4 and 5 the latter becomes so large that it obscures the first potential under it. The second potential is diphasic, and only occurs once after each shock. The first potential is the one repeated 3 to 5 times.

resting between spontaneous responses will respond vigorously. An optic-nerve stimulus at a given instant might therefore be expected to set into activity only those cells that were at that instant resting after their last spontaneous activity, but at *any* instant some cells would be resting and thus at no time would the cortex as a whole be unable to respond to visual impulses.

We find that either for electrical stimuli to the optic nerve, or for light flashes to the retina, weak stimuli cause a constant response only if delivered at the proper frequency, and at other frequencies, such stimuli find the cells which they attempt to activate refractory, while strong stimuli give responses at any frequency. We know that in the case of electrical stimuli, the

larger the fiber, the lower its threshold, and therefore a weak impulse must activate only the larger fibers of the optic nerve. From the similarity between the action of electric shocks and light flashes, we may infer that the larger fibers are the ones that connect with the more sensitive end-organs in the retina, which respond to weak light. We therefore conclude that the group of larger fibers sends impulses to a group of cells in the cortex which act in phase with each other, while a group of somewhat smaller fibers connects with cells which are active at different times from the former, but are also in phase with one another; a strong stimulus, activating all sizes of fibers, will thus always find some groups capable of responding.

The activity of the cortex is highly dependent on an adequate blood supply. If a vessel is clamped off, the part supplied becomes inactive in a very few minutes. The pressure of an electrode resting on the cortical surface may gradually render that point inactive, restoration of activity occurring promptly when the pressure is removed. If for any reason the animal's circulation is impaired (as, for instance, by falling blood pressure), cortical responses decrease, so much so that the record obtained on the oscillograph is an adequate index of the animal's general condition. Anesthesia also reduces the response; light anesthesia, sufficient to numb the animal, having, however, very little effect. As the depth of anesthesia is increased, the first sign is a lowering of the amplitude of the response to specific optic-nerve stimulation. Further anesthesia abolishes this specific response, at which stage the spontaneous activity has been reduced to perhaps one half its initial level. Response of the cortex to optic-nerve stimulation is abolished at about the stage that body reflexes disappear. Spontaneous responses fail at about the stage of failure of respiration. This series of effects, comparable as it is with effects on reflexes elsewhere in the body, indicates the similarity between the optic pathway and other sensory pathways, and suggests that the optic pathway, even though developmentally

a part of the brain itself, may, from the point of view of its neurophysiological behavior, act according to the rules that apply to other nerve mechanisms; the complications in its activity being mechanical ones, due to the complexity of elements, rather than to the physiological uniqueness of any one of its elements.

When the optic-nerve stump is given a single electrical shock, sending a volley of impulses, one in each fiber activated, up the optic nerve to the thalamus, the response recorded from the cortex varies in two ways. The first has already been commented on; namely, as strength of shock is increased, and more fibers thus activated, the responses first vary in height and finally become maximal and of equal size. But, secondly, as the shock strength is further increased, the latent period of the response decreases, and the form becomes more complex. The fact that the latent period decreases shows that spatial summation is taking place; that is, activity in one fiber pathway facilitates the activity in other pathways. The response in any one fiber being all-or-none, an increase of shock strength would not alter the activity of any one fiber that was activated at all; therefore an earlier response when more fibers are activated indicates a mutual assistance at synaptic levels, where the response of one fiber must therefore affect several synapses, and further, must affect the synapses to which other fibers also lead.

The increase in complexity of cortical response takes place as follows: At threshold, a small wave appears, 30 to 40 thousandths of a second after the shock (fig. 6, D.) Conduction in nerve fibers should account for not over one-thousandth; the rest must be delay at synapses. As the stimulus is increased, this response occurs earlier, and it can then be seen, at slightly above threshold, that other responses follow the first. There may be from three to five successive responses to one shock visible at intervals of  $\frac{1}{3}$  to  $\frac{1}{5}$  seconds, depending on the state of the animal. These responses are generally monophasic; that is, the deflection is all in



one direction from the base line. As the stimulus is still further increased, a second type of response is superposed upon the first wave of the first response, and since this develops a considerably greater voltage, it soon obscures the first as the shock is made stronger. This second type of response is diphasic, a deflection in a positive direction followed immediately by a deflection in the negative direction, and is not repeated as is the first, but is still followed by the later monophasic elements of the first series. With stronger shocks, the latent period decreases to a minimum of not over five thousandths of a second. Allowing about one thousandth for nerve-fiber conduction, and counting at least two synapses passed by the impulse started in the optic-nerve fibers, one at the thalamus and one at the cortex, this leaves not over two thousandths of a second per synapse.

We have described, so far, certain electrical responses of the optic nerve and of the cortex. We know less about the thalamus, since to expose this satisfactorily requires gross interference with parts that function with it. The optic thalamus can be observed to be rhythmically active, like the cortex, even when the optic nerve is not stimulated, and it seems probable that the activity of the cortex, spontaneous as well as that due to nerve stimulation, is largely controlled by the thalamus. We may infer, moreover, from what is sent into the thalamus over the optic nerve, and from what comes out at the cortex, something of what must have happened between. It is apparently here that summation takes place, where the effects of impulses too weak in themselves to cause a cortical response, are added up with other impulses, over different fibers, or at different times, until the total result can reach the cortex.

The electrical responses of the retina consist of several parts, superimposed so that it is difficult to tell which elements of the retina cause which response. An initial negativity, following exposure to light, is reversed to a positivity after a few thousandths of a second. Granit has recently shown that the

negative element persists while the retina is exposed to light but there is superimposed on it a positive wave presumably due to a different process. That the process which causes the initial negativity is the one which stimulates the optic-nerve fibers may be judged from the time relations of the response. The cortical response to a flash of light may occur earlier than the retinal positivity.

With a technic at hand for recognizing the activity of the various nervous elements of the optic pathway, the results of stimulation by flashes of light of different intensities and durations may be observed, as a nearer approach to normal functioning than is electrical stimulation of the optic nerve. By a system of revolving shutters and suitable lenses, a light source of any form or size can be focused upon the retina, its brightness regulated over any desired range, and the duration controlled from a fraction of a thousandth of a second up. Under light anesthesia, just sufficient to numb the animal, such flashes result in cortical activity, and the greater the quantity of light falling within a given time, the greater the response. The result is similar whether the quantity is varied by change of intensity or of duration. The result of increasing the quantity of illumination from threshold value is, first, to increase the voltage of the electrical activity, and second, to cause the cortical response to occur earlier after the stimulus.

A complication enters here, in the light scattered in the eye, falling therefore outside the true image. If a round image is focused on the retina, subtending  $7^\circ$  at the periphery, the remainder of the retina is faintly illuminated, at an intensity of about  $1/600$  of the image, measured photometrically from the back of the freshly excised, pigmented rabbit eye (not albino). Such a  $7^\circ$  area is about  $1/640$  of the area of the hemisphere of the eye. An image subtending a  $45^\circ$  angle gives a scattered brightness outside the image of  $1/12$ , and this intensity increases with the size of the image. Close to the edge of the image the "scattered" brightness is even greater. At any value of stimulus consider-

ably above threshold, the scattered light introduces an error of measurement, and a lack of sharp definition as measured by cortical action currents. One can not assume, therefore, that increasing the area illuminated increases in simple proportion the number of fibers activated, even though visual definition might still be sharp in terms of contrast.

These changes in response are due to the peculiar properties of the synaptic junctions between nerve units, and not primarily to the properties of nerve fibers themselves. If a nerve fiber responds to a stimulus at all, its response has a unit value, which does not vary in voltage nor in speed with the intensity of the stimulus. Sense organs, on the contrary, can be stimulated to respond more or less. The result of a stronger response of a sense organ is to cause the nerve fiber leading from it to respond more times in succession, and at greater frequency, each nerve response still being of the same value as if from a different stimulus. The *amount* of the response of the sense organ thus is represented by the *number of unit impulses* which its nerve fiber carries. At the next synapse, this number of nerve impulses is apparently again added up as a total quantity; if one nerve impulse is not enough to stimulate the next cell in the pathway, a second impulse added to it may be, and so on. Not only this, but if the impulse in one nerve fiber cannot stimulate the next cell, an impulse in another adjacent fiber can help it out, and if one impulse will stimulate the next cell only after a considerable interval of time, a second impulse following it immediately in the same fiber, or passing over another fiber, may cause the next cell to be stimulated sooner. This process presumably occurs at each synaptic level; at the retinal ganglion-cell layer, at the thalamus, and at the cortex; the sensory impulse changing back and forth from unit impulses in nerve fibers to total quantities at the synapses.

When a flash of light falls on the retina, the amount of light determines how much the sense organs are stimulated, and therefore how many impulses each fiber from each excited sense organ will

carry to the thalamus. The area illuminated will determine how many fibers carry impulses at all, and how large a part of the thalamus will be affected. The greater the quantity of light in the flash, the more nerve impulses will reach the thalamus, the sooner will the cells send their messages to the brain, and the more messages (nerve impulses) will be sent. By a repetition of this process at the cortical synapses, the sooner, and the larger, will be the cortical response observed, the greater the quantity of light on the retina.

There is a limit, however, to the shortening of the time required for cortical response. The nerve fibers require a certain time for conduction, and this is independent of the stimulus strength. A definite delay occurs at synapses, and there is a delay between the activation of the retina and the responses of nerve fibers from it, and a certain time is required for the light duration itself to stimulate, and these may all vary with the intensity of the stimulus. Starting with a flash of long duration but low intensity, the effects of increasing the intensity are, first, to activate the retina earlier during the stimulus, then, since the light will continue to act after the first impulses have left the retina over the optic nerve, further impulses following these will reinforce them at the thalamus level and shorten the time which would have been required for the first impulses alone to pass the synapses there. The time required for the cortex to respond will therefore be shortened in at least two places, probably more. The total variation in time of response may be 20 or more thousandths of a second, that is, from 30 to 50 or more thousandths (fig. 7).

If instead of varying the intensity, the duration of the flash is varied, a similar type of variation in time for cortical response occurs. Starting with a bright but very brief flash, a relatively long time may elapse (60 thousandths of a second), before the cortex responds. Increase of duration now shortens this time to a minimum of 30 thousandths. Since the retina must be activated during even the briefest flashes that cause a response, longer durations cannot

cause the sense organs to respond any sooner, but only more vigorously, and the variation in time of response in this case is presumably due to summation in nerve synapses rather than in the sense organs. In either case the shortening of response time is due to a greater total

electrical action currents, and as indicated by measurements of bodily response or of sensory occurrences in animals or human subjects. This does not mean that the cortical action currents recorded are those accompanying mental or psychological behavior. We are

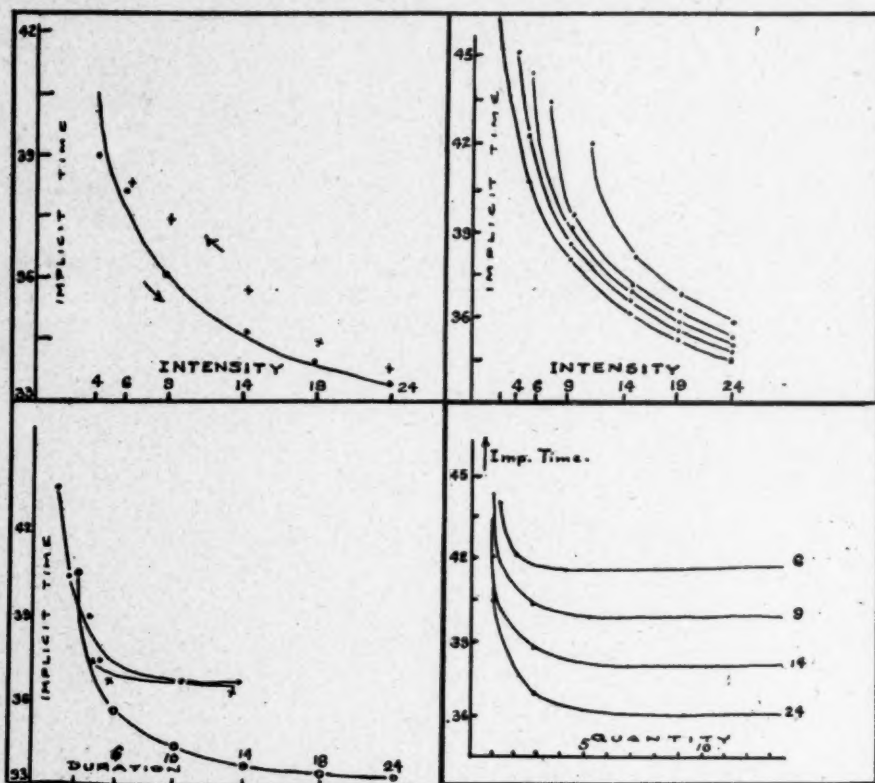


Fig. 7 (Bishop and Bartley). Upper left, curves showing the relation, in the rabbit, between stimulus intensity and the time it takes a visual impulse to reach the optic cortex ("implicit time"). Upper right, a series of curves as before, each from a different duration of stimulus. The abscissae are in terms of 100 candles per square foot, the ordinates in 0.001 second. Lower left, three curves, each from a different animal, showing the relation between stimulus duration (given in 0.001 second) and the time it takes a visual impulse to reach the optic cortex (time units in 0.001 second). Lower right, a family of curves showing the relation between the quantity of light (units in 0.001 second times 2400 candles per square foot), and the time it takes a visual impulse to reach the optic cortex (units of time in 0.001 second).

quantity of light, and within the limits of near-threshold values, increase of time of exposure to light acts quite like increase of intensity.

In many of the situations here discussed, close analogies could be drawn between the activity of the optic mechanism as indicated by measurements of

observing the nervous pathway of sensation, not the sensation itself. What correspondence there is between cortical activity and sensation does, perhaps, indicate that we are on the right track; that is, that the activity of the optic cortex we are observing is one stage in the modification or develop-



ment of the visual impulse on its way to cause sensation. We see that as the visual impulse passes over each level of its pathway its form is modified, its time relations changed. What happens to it beyond the surface of the optic cortex we do not know as yet, but in the thalamus and the cortex we can see that the impulse has met a condition not found in the peripheral structures. The impulse here arrives at a region which is already continuously active, whose activity does not depend for its initiation on an external stimulus such as light falling on the retina. It no longer finds nerve cells quiescent, waiting to be activated by it, but must deliver its energy into a network of cells that are already busy at something else. It seems probable that at this stage the visual impulse in a sense loses its individuality, and that from here on the act of seeing does not involve a simple passage of *visual* impulses over a specific pathway to a

definite center for seeing, but that it rather modifies the activity of cells already active, and by changing the pattern of activity of the cells of the brain, modifies its functioning. Possibly the mechanism of vision in the cortex is continually in activity, but its functioning is directed to certain results by sensory impulses from the outside, as any piece of machinery, with motors running but out of gear, might be put into purposeful activity by throwing levers and switches. This reverses, to be sure, the usual idea that the brain directs the periphery, but such a reversal is not without support from other fields of investigation. At any rate even if we succeed in observing in detail the nerve impulses coming over the optic tract to the cortex, the phenomena of vision will not be understood even in physiological terms until we understand more about the physiology of the cortex.

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*Discussion.* DR. LEO L. MAYER (Chicago): What relation, if any, is there between the essayists' findings and the double chronaxie of the optic nerve? What was your idea of the optic-nerve action in the experiments which you have done?

DR. GEORGE H. BISHOP: Since there are

two groups of fibers in the optic nerves with two action currents, and since there are two groups of responses from the cortex, we suppose there are two kinds of vision represented in the retina. We haven't found them yet but I suppose that may be correlated with the two chronaxies of the retina to light.

## NOTES ON THE ALLERGY THEORY OF SYMPATHETIC OPHTHALMIA

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This study was undertaken with the aim of discovering whether the histologic findings in sympathetic ophthalmia were compatible with the allergy theory of this disease. The relation of melanin granules to the specific histologic features of the inflammation in the uveal tracts, retina, and skin revealed that allergy to uveal pigment is an adequate explanation of these characteristics. However, allergy to uveal pigment may be present without sympathetic ophthalmia. If the allergy theory is correct some additional factor other than allergy is, therefore, necessary to initiate the disease. A study of the Dalen nodules sometimes found in sympathetic ophthalmia suggests that the additional factor may be a proliferation of the melanophores. The results of some preliminary experiments based on this hypothesis are reported.

From the Wilmer Ophthalmological Institute of the Johns Hopkins University and Hospital. Read before the Association for Research in Ophthalmology, in Cleveland, June 12, 1934.

The allergy theory of the pathogenesis of sympathetic ophthalmia, first suggested by Elschnig<sup>1</sup> and strongly supported by the work of Woods<sup>2</sup>, and others, occupies a position so unique among general theories of pathogenesis of disease that it seems strange that many of its postulates and corollaries have not been subjected to a penetrating analysis. To the pathologist who attempts to work out rational connections between conceptions of pathogenesis and morphologic characteristics of disease, numerous questions arise in contemplating sections of eyes suffering with sympathetic ophthalmia. It is my purpose, in the present paper, to state some of these questions, and to show in how far the problems which they raise may be reconciled with the allergy theory.

In a recent series of studies, Samuels<sup>3</sup> has attempted a similar analysis of the histology of sympathetic ophthalmia in relation to the infection theory as to its origin. He has shown that in many cases, there is a well-circumscribed lesion at the site of the initial penetrating wound, which may be regarded as the primary lesion, while the remainder of the reaction in the inciting eye can usually be traced as a direct extension of the primary lesion. Such is, indeed, what one might expect on the basis of the infection theory of the disease, provided the infectious agent were bacterial, for, in many instances, the spread of bacterial lesions is by direct extension. The lesions produced by vir-

uses, on the other hand, do not show an equal tendency to spread by contiguity.

It must be clear that no evidence of this sort, neither that advanced by Samuels nor that which I am about to present, is adequate to establish either the infection theory or the allergy theory of the disease. Such evidence, in fact, can have only negative weight, in the sense that if evidence is found that is incompatible with the present state of the theory, then the theory must be either abandoned or modified. There is, however, a positive aspect to the question. If a theory is correct, it should be possible by logical deduction from it to reach conclusions that may be confirmed by observation. We hope to show that this is possible in relation to the allergy theory of sympathetic ophthalmia. While this does not prove the theory to be true, it does demonstrate that it has heuristic value and, as such, merits very earnest consideration. It is with this in mind that I submit the following more or less disconnected notes on the histology of sympathetic ophthalmia.

### General Aspects of the Histologic Picture

The histologic picture of sympathetic ophthalmia is so similar to that of diseases of known infectious etiology, such as tuberculosis, as to raise grave doubts concerning the unique pathogenesis of the former. The evidence seems to be written all over these sections that an infectious agent could



Fig. 1 (Friedenwald). Sympathetic ophthalmia, showing pigment phagocytosis by epithelioid cells and giant cells. (Low power.)

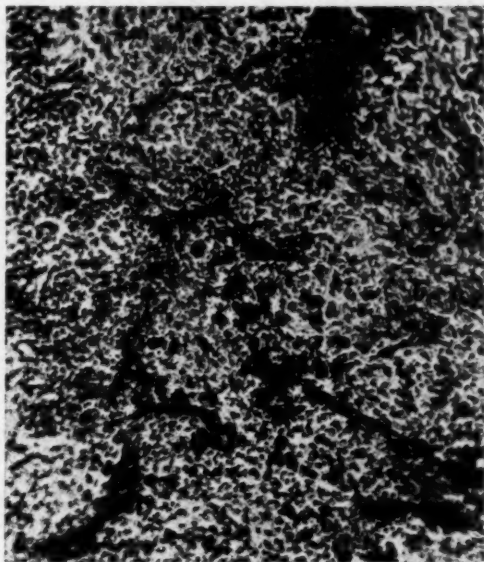


Fig. 3 (Friedenwald). Sympathetic ophthalmia, showing pigment phagocytosis by epithelioid cells and giant cells. (Low power.)

cause the condition. But what is it that we see in the histologic study of infected tissues other than those reactions of the host that are in whole or in part related to allergy? Some infectious agents, it is true, produce a toxin that may cause direct, visible injury to the

tissues. Other infectious agents elicit at some stages, at least, a nonspecific foreign-body reaction. In tuberculosis, however, the histologic features seem to be dominated by allergic reactions, and if allergy in tuberculosis is abolished, little remains of its characteristic his-

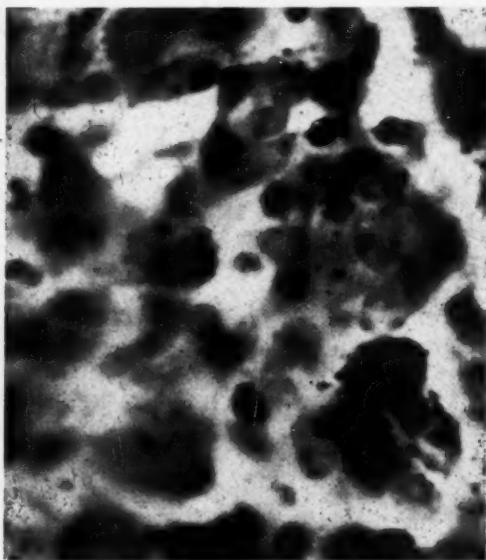


Fig. 2 (Friedenwald). Same as figure 1. (High power.)

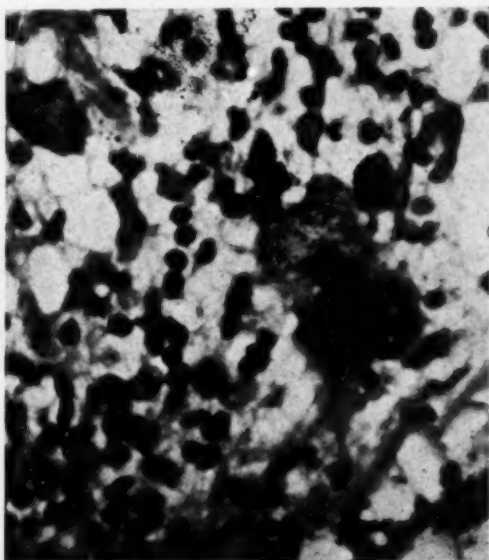


Fig. 4 (Friedenwald). Same as figure 3. (High power.)



tologic picture except a few giant cells and epithelioid cells<sup>4</sup>. There is then, *a priori*, no reason why a histologic reaction resembling that of tuberculosis should not be completely determined by allergy. Indeed, it has been possible with the aid of tuberculin, dead bacilli, etc., to produce in sensitized animals allergic reactions histologically indistinguishable from those of active tuberculous lesions.

### Pigment Phagocytosis

According to Koch's postulate, a specific organism cannot be established as the specific cause of an infectious disease unless that organism can be found in the specific inflammatory lesions of that disease. By analogy, one should require that, in a disease thought to be allergic, the specific antigen should be regularly demonstrable in the specific lesions. If uveal pigment is the antigen responsible for the histologic reaction in sympathetic ophthalmia, one should be able to find pigment granules within the phagocytic cells at the centers of the lesions. This is, indeed, the fact. Careful study shows that the epithelioid cells, and especially the giant cells in sympathetic ophthalmia, are loaded with pigment. I have compared the pigment phagocytosis in cases of sympathetic ophthalmia with that in ocular tuberculosis: in sympathetic ophthalmia it is always widespread and abundant; in tuberculosis, it is often wholly absent, and, when present, is clearly related to destructive lesions, e.g., caseation, of the uveal tissues.

This distinction can be brought out even more clearly if one studies sections stained specifically for melanin granules. For this purpose, the usual silver stain can be used which converts into black granules not only those which in unstained preparations obviously contain melanin, but also colors the so-called premelanin granules in melanin-bearing cells. Similar results can be obtained with Brown's bacterial stain<sup>5</sup> with which the melanin and premelanin granules take on an intense gram-positive stain. Normal eyes stained in this manner show an abundance of granules

within the melanophores of the uvea and the pigment epithelium, even in blonde individuals. In inflammatory diseases of the eye other than sympathetic ophthalmia, the stained granules are not found outside the cells which normally contain them, except in relation to lesions in which there has been tissue necrosis. In sympathetic ophthalmia, the epithelioid cells and giant cells throughout the uveal tract are loaded with stainable granules. It is to be noted, furthermore, that where pigment phagocytosis occurs in nonsympathetic affections, the granules are usually, though not always, contained, densely packed, in rounded, monocytic cells which may be either large mononuclear cells or migrating melanophores, while in sympathetic ophthalmia, the granules are to be found in the epithelioid cells and giant cells.

I have studied these points particularly in relation to tuberculous lesions in the eye, since I happened to have a large series of guinea pigs in which ocular tuberculous lesions had been experimentally produced. The total absence of pigment phagocytosis in those eyes in which there was no tissue destruction was most striking. Equally clear was the limitation of pigment phagocytosis to the regions surrounding necrotic and caseous lesions, when these were present. The distinction has, in my experience, been so regular and clear cut as to form a useful differential diagnostic aid.

The wide-spread presence of pigment granules in the epithelioid cells in cases of sympathetic ophthalmia was observed by Fuchs<sup>6</sup>, who left little unnoticed in his description of this disease. Fuchs, however, interpreted this as indicating that the epithelioid cells were derived from the chromatophores, a conclusion which modern studies on histogenesis would not easily support. If the epithelioid cells were, in fact, derived from melanophores and not merely laden with their detritus, pigment should be equally widely disseminated amongst them in the lesions of ocular tuberculosis.

The importance of pigment phagocytosis within the uveal tract may, per-

haps, be subject to some discount since this phenomenon occurs, though to a much less degree, in other inflammatory lesions. It seems desirable, therefore, to discover whether specific inflammatory lesions could be found in other tissues also containing pigment phagocytosis. The frequent presence of characteristic episcleral inflammatory nodules in sympathetic ophthalmia is well known, and in these also the epithelioid cells and giant cells are loaded with pig-

ments, these lesions contained conspicuous numbers of melanin granules. The presence of pigment deposits in the retina is, of course, not uniquely a feature of sympathetic ophthalmia. Masses of pigment are transported into the retina in any destructive lesion of the pigment epithelium or choroid. In such cases, however, the pigment is regularly found in dense compact clumps within rounded monocytic cells or, as in retinitis pigmentosa, within phagocytic retinal

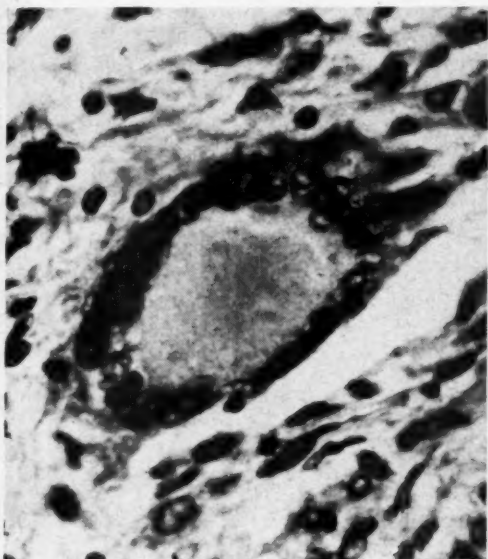


Fig. 5 (Friedenwald). Giant cell in tubercle of the choroid without any pigment phagocytosis.

ment. It is to be remembered, however, that small numbers of melanophores are frequently found in the episcleral tissues.

More significant are the inflammatory nodules which may be found in the retina. Out of twenty-two cases of sympathetic ophthalmia, in this laboratory, and twenty-five cases in the Army Medical Museum, I was able to find six which showed small epithelioid and giant-cell nodules in the retina. In all of these cases, the retina was detached. The inflammatory nodules were usually located in the outer layers of the retina, but in some instances, they invaded its whole thickness. As in the uveal tract, the epithelioid cells and giant cells in

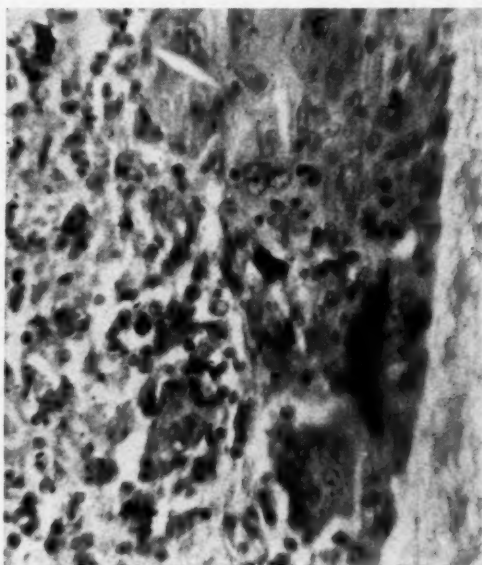


Fig. 6 (Friedenwald). Sympathetic ophthalmia, showing an epithelioid-cell and giant-cell nodule in the detached retina, with marked pigment phagocytosis in the nodule.

neuroglia cells<sup>7</sup>. In either case, the deposit of pigment in the retina is not surrounded by any conspicuous inflammatory nodule. The remarkable feature in sympathetic ophthalmia consists in the fact that whenever melanin pigment is deposited in the retina, the granules are engulfed by epithelioid cells and giant cells and surrounded by an inflammatory infiltration which has all the characteristic features of the specific lesions of sympathetic ophthalmia.

In this connection it is of interest to report the findings in a healed case of sympathetic ophthalmia. The patient was a girl who, at the age of three years, stuck a scissors into her left eye. A

typical bilateral uveitis appeared four weeks after the injury. Eventually, the injured eye became phthisical, while in the sympathizing eye, most extensive posterior synechia developed, followed by cataract formation. Her physician attempted to extract the cataract, but the pupil became closed by a very dense membrane and vision was reduced to light projection in the sympathizing eye, with no light perception in the injured eye. I saw the child first when she was eight years old. There had been no evidence of active inflammation in either eye for several years, and it was thought that, in view of the good light projection in the right eye, an operative attempt was justifiable. Preparatory to this, the totally blind and shrunken injured eye was enucleated. Histologically, this eye showed the usual features of phthisis. It was shrunken to about two-thirds normal size. The remains of the lens and the detached retina were matted together in a dense cyclitic membrane. No trace of any active cellular infiltration was found in the sections. Of special interest was the uveal tract, which showed little gross distortion of its structure, but which was completely replaced by scar tissue within which not a granule of uveal pigment was to be found. If the allergy theory of sympathetic ophthalmia is correct, this remarkable finding may be interpreted as indicating that in some instances the healing of the lesion is accompanied by the total removal of the effective allergic antigen.

#### **Skin Tests with Uveal Pigment**

The second of Koch's postulates requires that the specific infectious agent should be demonstrated experimentally to produce the typical lesion of the infectious disease in a susceptible animal. The analogous postulate to be met by the allergy theory of sympathetic ophthalmia would consist in producing the specific histological characteristics of sympathetic ophthalmia in an animal allergic to uveal pigment. Unfortunately, no one has, so far, succeeded in sensitizing experimental animals with uveal pigment of their own or other species. Elschnig was able to produce

anaphylactic shock in guinea pigs on repeated injection of a pigment suspension derived from rabbits. He was also able to produce complement-fixing antibodies in the serum of animals injected with emulsions of uveal pigment, which could be bound by pigment derived from members of their own as well as other species. These observations were confirmed by others and extended by Woods. That uveal pigment represents a tissue-specific antigen can, therefore, hardly be doubted. The demonstration of the specific antigenic quality of a particular material is, however, a very different matter from the production of an allergic inflammatory reaction in the tissues of a sensitized animal. The latter is always a matter of considerable experimental difficulty. We do not know, except in a vague and purely empirical way, what are the factors that result in one animal in the appearance of precipitins or complement-fixing antibodies in the blood following parenteral injection of foreign protein, while in another, the tissues manifest a hypersensitivity in the form of an inflammatory reaction to the second injection of the foreign substance. Species susceptibility and the antigenic potency of the foreign material seem to play a rôle, but the experimental conditions required to elicit the allergic inflammatory reaction vary in an unpredictable manner from one antigen to the next. It has, for instance, only in the last few years, been found possible to sensitize animals to tuberculin without the injection of either living or dead tubercle bacilli. It is no wonder, therefore, that tissue sensitization to relatively inert and insoluble melanin granules has not yet been experimentally produced, and the failure on this score does not negate the antigenic capacities of this material.

Barring the experimental approach to this problem, it is still possible to perform a similar study through an analysis of the tissue reactions in patients suffering with sympathetic ophthalmia to the intradermal injection of suspensions of uveal pigment. For some years, Woods has used such skin tests as a diagnostic procedure in cases of sympathetic ophthalmia. He reports



that in these cases almost always some redness and induration show at the site of inoculation, 24 to 48 hours after the injection, whereas all normal controls and almost all individuals suffering from a nonsympathogenic inflammation of the eyes, give negative reactions. The test is, however, not an easy one to interpret, for the typically "positive" reactions are by no means conspicuous. This is not to be wondered at, since, in

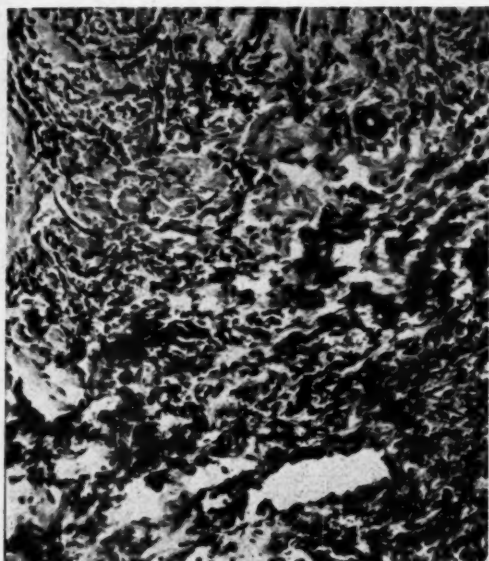


Fig. 7 (Friedenwald). Negative skin test for uveal pigment. The biopsy was performed on a normal person two weeks after intradermal injection of a suspension of uveal pigment. There is still some unphagocytosed pigment in the lower-left-hand corner of the picture. The surrounding tissues are infiltrated with lymphocytes and large round cells. The latter have ingested so much pigment that they are jet black.

the eyes, the sympathetic inflammation is generally characterized by the relative mildness of its vasomotor reaction in comparison with the massive quality of its cellular infiltration. It seemed desirable, therefore, to study these reactions histologically, so material was obtained by biopsy in a number of cases, as follows:

In the first instance, it was thought necessary to discover at what time following injection the most characteristic differences were to be found, and tissue was removed from the skin of a patient

suffering from sympathetic ophthalmia 1, 2, 7, and 14 days after the injection of uveal pigment\*. These samples were compared with the similar series obtained from three patients who were not suffering from any intraocular inflammatory disease. The skin tests in the sympathetic case were definitely positive by the usual clinical criteria, those on the normal controls were entirely negative. The histologic study



Fig. 8 (Friedenwald). Negative skin test for uveal pigment, showing the large round cells filled with pigment granules. (High power.)

revealed no difference between the specimens removed 24 and 48 hours after injection. In all of these, the pigment was found in a large formless mass in the fibrous tissue of the chorium. Surrounding the mass of pigment, there was a sparse rim of wandering cells, mainly monocytes, which were beginning to phagocytose the pigment. The number of these cells was, perhaps, somewhat greater in the sympathetic-ophthalmia case than in the controls, but the difference was not conspicuous. Any edema that may have been present in the sympathetic-ophthalmia case was obscured by the local injection of novo-

\* Suspension prepared according to the technic of Woods\*.

cain and adrenalin, which was used in obtaining the biopsy.

In the specimens taken one, and still more in those taken two weeks after in-

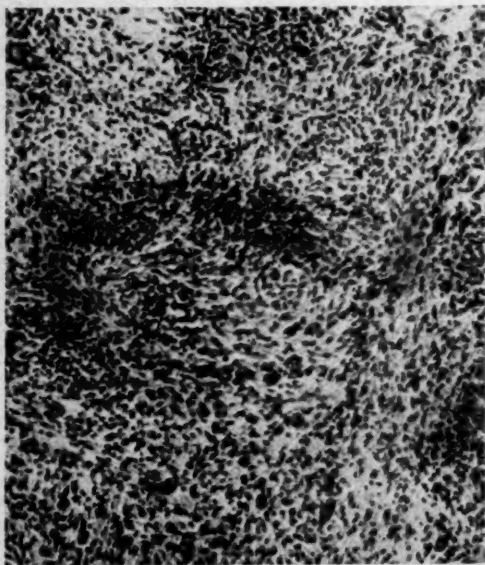


Fig. 9 (Friedenwald). Positive skin test for uveal pigment from a case of sympathetic ophthalmia, showing a large epithelioid-cell nodule with scattered masses of phagocytosed pigment.

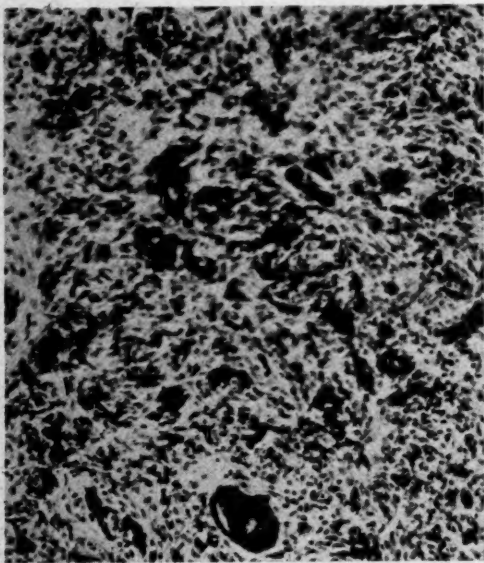


Fig. 10 (Friedenwald). Positive skin test for uveal pigment in a case of sympathetic ophthalmia, showing epithelioid cells and giant cells loaded with pigment.

jection, a marked difference was found between the reactions of the sympathetic-ophthalmia case and those of the normal controls. The latter, even at the end of two weeks, still showed large masses of unphagocytosed pigment. These were surrounded by a zone of large mononuclear cells filled with pigment granules. Beyond this, was a sparse zone of lymphocytes. The extent of the reaction from the margin of the pigment deposit to the outer zone of lymphocytes was about one-half millimeter. Outside this zone, the tissues showed no reaction. There was no perivascular infiltration outside the nodule. In contrast to this, the tissue from the case of sympathetic ophthalmia showed no remaining extracellular pigment, and the pigment mass had been spread apart by a massive infiltration of epithelioid cells and giant cells within which the pigment was to be found. The nodules measured several millimeters in diameter and were surrounded by a zone of lymphocytes with perivascular round-cell infiltrations extending to the limits of the section. The histologic picture of the epithelioid-cell nodule was indistinguishable from that of the ocular reactions in sympathetic ophthalmia.

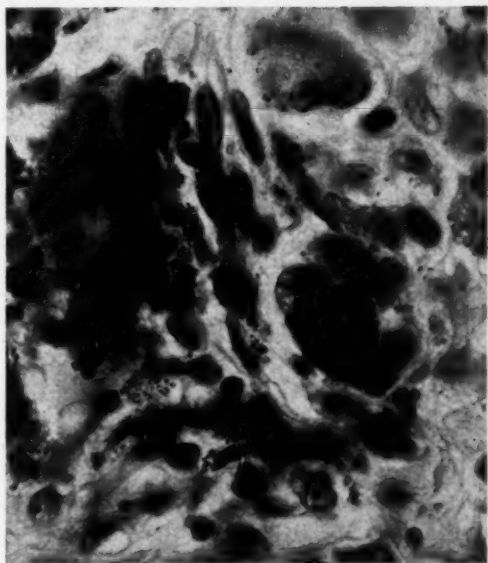
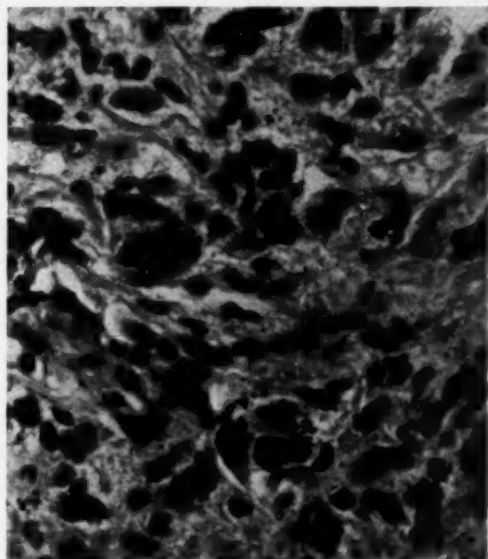
Following this preliminary test, the routine has been adopted to remove tissue for study two weeks after the intradermal inoculation of uveal-pigment suspension. Five cases of active sympathetic ophthalmia have been available for examination and, in all, the histologic characteristics of the lesion have been the same as those described above. In eight controls who had had no injury to their eyes nor any intraocular inflammatory disease, the negative reaction described above was found regularly repeated. In two cases of old healed sympathetic ophthalmia, similar negative reactions were obtained. The test was also made in seven cases of chronic non-symphathogenic uveitis. In four of these the reaction was negative. In three cases, which were clinically diagnosed as tuberculous, the reaction was slightly more marked than that which has been described as negative. In these, very little unphagocytosed pigment re-

mained in the tissue, and while the predominant infiltrating cells were large, round, mononuclear cells, a few nests of epithelioid cells were found, and some slight perivascular infiltration was seen one or two millimeters from the main lesion. Finally, one false positive case was encountered. This case has already been reported by Woods<sup>9</sup>, and the details of the clinical course will be repeated here. The patient had had a penetrating wound of the eye, which healed without complication. The skin test with uveal pigment was found to be strongly positive on clinical examination, and on histologic study could not be distinguished from the tissue obtained from sympathetic-ophthalmia cases.

Since the histologic characteristics of the skin reaction in the cases of sympathetic ophthalmia were indistinguishable from those of the specific lesions of this disease, one must conclude that allergy to uveal pigment is adequate to explain the characteristic histologic features of this disease. The postulate analogous to Koch's second, which was formulated above, has been satisfied, for the characteristic lesions of the disease have been reproduced in a susceptible individual by the local injection of the presumed specific antigen. The occurrence of the false positive reaction, however, makes it clear that allergy to uveal pigment alone is not sufficient to elicit the disease. Some other factor must be necessary to render the pigment available for the allergic reaction. Woods has recognized the necessity for such an added factor and concluded that "there was a definite allergic phase in sympathetic ophthalmia, but it did not appear this was the only cause of the disease and other etiological factors might well figure in the condition." Up to the present, suggestions as to what the additional factor might be have been limited to the notion of concomitant bacterial infection, and various organisms have been mentioned as possibly responsible. It is proposed in the next section to formulate a totally different hypothesis regarding this other necessary factor in the causation of the disease.

#### Proliferation of Melanin-Bearing Cells

Whenever the retina is detached for a prolonged period, small foci of proliferation develop in the layer of pig-



Figs. 11 and 12 (Friedenwald). Positive skin tests for uveal pigment. (High power.)

ment epithelium forming the familiar "Drusen." When this happens in the absence of sympathetic ophthalmia, the proliferating cells produce masses of hyalin which may be later calcified, and



the whole process goes on without the slightest inflammatory reaction. In sympathetic ophthalmia, on the other hand, these proliferating nodules of pigment-bearing cells undergo dissolution, and become infiltrated with epithelioid cells and giant cells. These inflammatory nodules in the pigment epithelium have been known for a long time. They were first described by Dalén<sup>10</sup> and later



Fig. 13 (Friedenwald). Small Dalén-Fuchs nodule in a case of sympathetic ophthalmia.

by Fuchs<sup>6</sup>. They occur usually when the retina has been detached; in the absence of detachment, the pigment epithelium almost always is spared the inflammatory reaction. The relation of the Dalén-Fuchs nodules to the ordinary Drusen is, therefore, quite clear.

It is, I think, most instructive to compare these nodules with the adjoining cells of the pigment epithelium. Within the nodules, the proliferated cells have undergone autolysis. Their pigment has been scattered about and picked up by epithelioid and giant cells, which invade the nodule and form inflammatory lesions that show all the characteristic features of the disease. The neighboring cells of the pigment epithelium show no abnormality and are not involved in the inflammatory reaction.

This finding suggests a possible hypothesis regarding the unknown accessory factor required for the development of sympathetic ophthalmia under the allergy theory. The hypothesis may be formulated as follows: In some cases following an injury to the eye, the body becomes hypersensitive to uveal pig-

ment. This alone is not sufficient to elicit the disease, for cells containing melanin granules show no abnormal reaction, in their resting state, to the presence of allergic antibodies. When, however, such cells proliferate, they become vulnerable to the antibodies and undergo autolysis, releasing their melanin granules, which, in time, elicit the allergic inflammatory reaction.

While this hypothesis is at present inaccessible to experimental test, it nevertheless furnishes a convenient framework with which to connect many of the more obscure features of this disease. It has, for instance, long been one of the stumbling blocks of the allergic theory that this theory required the

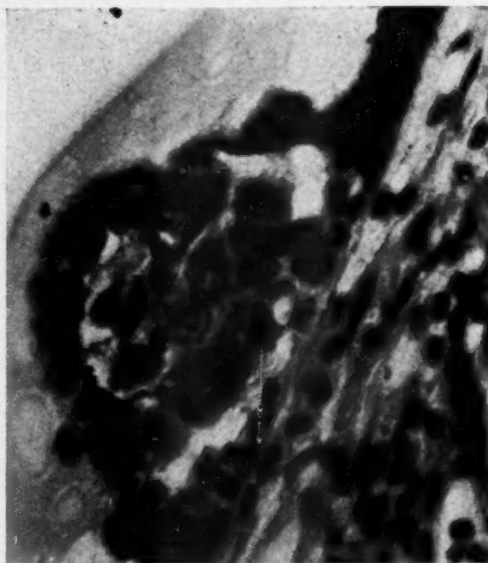


Fig. 14 (Friedenwald). Same as figure 13, showing the disintegrating cells of the pigment epithelium on the surface of the nodule and the phagocytosis of their pigment by invading epithelioid cells and giant cells. (High power.)

cells of the body to become reactive to some of their normal constituents, a phenomenon that has been characterized disparagingly as "Horror Autotoxicus." No such intracellular autotoxic reaction has ever been demonstrated with melanin pigment nor any other substance. Our present hypothesis considerably reduces this difficulty, for the metabolism and permeability of

cells change very markedly during proliferation, and proliferating cells are known to be much more readily injured by a variety of agents than are resting cells. This hypothesis also provides a reasonable explanation for those rare cases of intraocular melanoma which become complicated by sympathetic ophthalmia, and which are indeed very difficult to explain with the infectious theory. The fairly frequent occurrence of leukodermic patches on the eyelids, in cases of sympathetic ophthalmia, may also be related to this hypothetical course of events.

In the absence of any proof as to the correctness of this hypothesis, it is idle to speculate as to the mechanism that might be involved in stimulating proliferation of the melanophores. It may, however, add to the plausibility of the hypothesis to recall that there is ample demonstration of the fact that in amphibia and lower animals the melanophores are highly reactive to nervous and hormonal control, and that there is some evidence indicating that in mammalia, the pigmented cells in the eye are similarly reactive.

#### Therapeutic Test

If the hypothesis that we have suggested is correct, certain conclusions can be drawn that are of interest in guiding rational therapy. It is clear that, if the inflammation in the eye is due to an allergic reaction to uveal pigment, it would be desirable to supply the body with this pigment at some other site, so that the reaction would take place in tissues less vital to the organism, and thus bind the allergic antibodies with antigen presented elsewhere. This is the rationale of the attempt at therapeutic desensitization, which Woods has presented. It is, however, apparent, both from the clinical results of this method, which have not been very striking, and from the histologic study of the reactions to uveal pigment, which showed that it was a very insoluble and feeble antigen, that such a procedure must necessarily be a very slow and ineffective method of desensitization. On the other hand, if the melanin of the skin is, as we sus-

pect, closely related to, or identical with the melanin of the uveal tract, then a proliferation of the skin melanophores would provide the body with a readily available and widely distributed source of the specific antigen and a much more effective desensitization might be achieved.

On the basis of these assumptions, I have treated three patients having sympathetic ophthalmia with ultraviolet light, exposing their bodies to an erythema dose of the radiation three times a week with careful protection of their eyes and faces. The indicated local treatments and salicylates were, of course, given at the same time. Of the three cases, two were in children in whom the diagnosis was established by histologic study on the injured eye, and in whom the inflammation in the sympathizing eye was severe and progressive, before the ultraviolet treatments were begun. Both these children made complete recoveries. The third case was in an old gentleman with bilateral cataracts and senile dementia, who developed a typical bilateral uveitis following cataract extraction on one eye. He was given the treatment outlined above, and the inflammatory reaction became quiet, but both pupils were bound down by dense adhesions, so that his vision was reduced to light projection. Further operations could not be performed because of his mental condition and he had to be transferred to a hospital for the mentally incompetent.

This small series of cases is certainly inadequate as a test of the hypothesis. Furthermore, it is to be admitted that even if this treatment should prove to be regularly useful in sympathetic ophthalmia, it would furnish only indirect support to the hypothesis which led to its use. It is not, therefore, as evidence in favor of this hypothesis that I report this small group of cases, but because sympathetic ophthalmia is such a rare disease that one cannot hope, within a short span of years, to be able to study an adequate series of cases, and because it is such a terrible disease that a possibly beneficial and certainly harmless therapeutic suggestion should not be withheld from the profession.

### Conclusion

(1) The characteristic histologic features of sympathetic ophthalmia are compatible with the allergy theory of its etiology.

(2) Phagocytosis of melanin granules by epithelioid cells and giant cells forms a prominent feature of the lesions of sympathetic ophthalmia in the uveal tract, in the episcleral tissues, and in the retina, and is absent or insignificant in other intraocular inflammatory diseases.

(3) The reaction in cases of sympathetic ophthalmia to the intradermal injections of uveal-pigment suspension has all the characteristics of the inflammatory reaction in the eye.

(4) The skin reaction of normal controls and of patients with nonsympathetic uveitis generally differs from

that in cases of sympathetic ophthalmia.

(5) False positive reactions, however, were encountered, which make it necessary to conclude that, if allergy to uveal pigment is responsible for the characteristic lesions of sympathetic ophthalmia, some other factor is required to release the uveal pigment from the melanophores, and make it available for the allergic reaction.

(6) A study of the Dalén-Fuchs nodules, which are characteristic of sympathetic ophthalmia, leads to the hypothesis that the additional factor required for the initiation of the inflammatory reaction is a proliferation of the intraocular melanophores.

(7) Based on this hypothesis, a suggestion is offered in regard to treatment, which has been found apparently effective in a limited series of cases.

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## THE ETIOLOGY OF INCLUSION BLENNORRHEA

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From an experimental study of eleven cases, the author concludes that inclusion blennorrhoea is a distinct clinical entity, unassociated with any pathogenic conjunctival bacteria. It is not identical with trachoma, lacking the tendency to form pannus and scars. It is transferred to the conjunctiva of *Macacus rhesus* with difficulty, to the baboon more easily and with the induction of more acute symptoms. Other laboratory animals are resistant.

Microorganisms are seen in Giemsa-stained films of the secretion, decolorized in alcohol, in numbers in direct proportion to the clinical severity of the disease. The predominating forms are small and are known as elementary bodies, the larger as initial bodies; division forms of both are observable. Their staining reactions, alcohol fast but not acid fast and staining poorly with aniline dyes, constitute a differential point from ordinary conjunctival bacteria, being essentially those of rickettsiae, and of the elementary bodies of vaccinia, fowl-pox, and molluscum contagiosum.

The identity of these organisms with the etiologic agent of the disease has been proved. They are intracellular colonies of the virus in various stages of development, the initial body being the early stage, the elementary body the later phase. The life cycle comprises 48 hours.

The source of infection is genital, inclusion bodies having been found in vaginal secretion from the mothers of infected infants, and having from that source infected the eyes of monkeys.

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### Introduction

A benign form of conjunctivitis in the newborn infant, unassociated with pathogenic bacteria, has been recognized since the researches of Morax<sup>1</sup> in 1903. The finding by Heymann<sup>2</sup> of cytoplasmic inclusion bodies, similar to those in trachoma, in conjunctival scrapings from those affected by the disease, led to the name inclusion blennorrhoea (Lindner<sup>3</sup>). In spite of the extensive researches of Lindner, Botteri<sup>4</sup>, Heymann<sup>2</sup>, Löhlein<sup>5</sup>, Axenfeld<sup>6</sup>, Morax, Lindner, and Bollack<sup>7</sup>, and others, the etiology of the disease has not been established. The inclusion bodies have been variously considered as: (1) intracellular masses of the causal organism (Lindner<sup>3</sup>), (2) nonspecific reaction products (Gifford and Lazar<sup>8</sup>), (3) phagocytosed bacteria (Williams<sup>9</sup>, Stewart<sup>10</sup>), and (4) intracellular changes resulting from the activity of a filtrable virus (Lumbroso<sup>11</sup>).

### Historical Survey

Shortly after Halberstaedter and v. Prowazek<sup>12</sup> discovered inclusion bodies in trachoma, Stargardt<sup>13</sup>, and then Schmeichler<sup>14</sup> noted the presence of identical epithelial inclusions in conjunctivitis of the newborn, either with

or without the gonococcus. No importance was attached to these observations until 1909 when Heymann<sup>2</sup> reported at the Congress of Medicine at Budapest the results of his researches which had been made at the request of Uhthoff. He had attempted to determine the presence or absence of inclusions in a series of preparations from trachoma and other types of conjunctivitis, without knowledge of their origin. The result was that inclusions were found, not only in trachoma, but also in four cases of gonococcal infection of the newborn. These findings, joined with those of Leber and v. Prowazek<sup>15</sup>, who found inclusions in a conjunctivitis peculiar to the Samoan Islands, with those of Uhlenhuth and his coworkers<sup>16</sup>, who found inclusions in the conjunctivae of pigs ill with hog cholera, and with those of Pascheff<sup>17</sup> and of Flemming<sup>17</sup>, who found inclusions in a form of conjunctivitis of the adult, tended to shake the conviction of the specific role of the inclusion bodies in trachoma.

In 1909, Lindner<sup>3</sup> undertook the study of conjunctivitis of the newborn and showed that the inclusions were found with few exceptions only in that

form of conjunctivitis (*conjonctivite amicrobienne*) which Morax<sup>1</sup> had already differentiated from gonococcal conjunctivitis and the other types of conjunctivitis of known bacterial origin. In a series of 120 cases, the coexistence of the inclusion bodies with gonococci was found only four times. Lindner successfully inoculated the conjunctiva of the baboon, noted the presence of epithelial inclusions, and named the disease "Einschluss Blennorrhoe" or inclusion blennorrhea. In 1911, Morax<sup>1</sup> collaborated with Lindner and Bollack to confirm the existence of this conjunctivitis and its transmissibility to the monkey.

In 1910, Wolfrum<sup>17</sup> described two inoculation experiments of the adult with secretion from cases of inclusion blennorrhea. In the first subject, an incubation period of one week was followed by conjunctival inflammation, and on the ninth day numerous inclusions were found. The evolution of the case, according to Wolfrum, who unfortunately gave no details, was that of a true trachoma. In a second experiment, the subject was anophthalmic but had a normal conjunctiva without inclusions. Conjunctival hyperemia developed on the fifth day after inoculation and on the eighth day there were secretion and beginning follicle formation. After the twelfth day, epithelial scrapings showed some inclusions. The evolution was more benign than in the first case.

Searching for the origin of this disease of the newborn, Halberstaedter and Prowazek<sup>17</sup> found typical inclusions in scrapings from the urethral apertures of two mothers of diseased infants. On the basis of these findings, they formulated the theory of an inclusion disease of the male and female genito-urinary tracts. Support for this theory soon came from Lindner<sup>17</sup>, who found inclusions, though in small numbers, in several cases of urethritis and from Heymann<sup>17</sup>, who found inclusions together with gonococci in both parents of a child having inclusion blennorrhea. Later Fritsch, Hofstaeter, and Lindner<sup>18</sup> inoculated the eye of a baboon with the urethral exudate from a case of nongonococcal urethritis of 14 days'

duration. The urethral exudate was scanty but contained typical inclusion bodies. Three days after inoculation the conjunctiva of the baboon became hyperemic and on the fourth day secretion developed. After the eleventh day, inclusions were numerous. By the twentieth day, there was a follicular conjunctivitis which lasted several months.

Wolfrum concluded that the disease resulting from his inoculations was identical with trachoma, a conclusion shared by Lindner, who described it as a "genital trachoma." Gebb<sup>19</sup>, on the other hand, in repeating Wolfrum's experiments, demonstrated that the adult disease so produced could in no way be confused with trachoma. Eight subjects so inoculated developed an active but self-limited disease, which healed without pannus or scars in less than a year. Löhlein noted that while inclusion blennorrhea was easily transmissible to the monkey, trachoma was transmissible only with difficulty. He stated his belief that there existed an inclusion conjunctivitis of the adult entirely analogous to inclusion blennorrhea, distinct from trachoma, but corresponding in part to the cases often described as doubtful or benign trachoma.

The filtrability of the disease was claimed by Gebb, who inoculated a human subject with a Berkfeld filtrate of a suspension of virulent material in physiologic salt solution, kept for one hour at room temperature. A disease developed on the fourth day, similar in appearance and clinical course to the disease that had been produced by unfiltered material. A confirmatory result on the eye of a baboon was obtained by Botteri<sup>4</sup> who used a Berkfeld filtrate of a suspension of conjunctival scrapings from an affected infant.

Since the World War, inclusion blennorrhea has received very little attention. James<sup>20</sup>, in 1930, reported four cases in 2446 deliveries at the St. Louis Maternity Hospital, with onset the 5th, 8th, 11th, and 13th day after birth. Direct smears and scrapings were negative for bacteria, and cultures revealed only *C. xerosis* and *Staph. albus*. On the twelfth day after inoculation a rhesus

monkey developed follicles which persisted over a period of 7 months. No inclusions were demonstrable in scrapings. James mentions the accidental infection of one mother from her child on the 28th day post partum. In a report published in 1933, Stewart<sup>10</sup> concluded that inclusion blennorrhea had no existence as a separate disease, but was gonococcal ophthalmia in which the inclusions were nests of phagocytosed gonococci. Since analysis of his report discloses that Stewart had never personally seen a case of inclusion blennorrhea, his conclusions must be discarded as of no significance. The monograph of Lumbroso<sup>11</sup>, based on a study of 17 cases, is the most recent work on the subject. Lumbroso concludes that inclusion blennorrhea, which he prefers to call granular blennorrhea (blennorrhée granuleuse) is a specific conjunctival disease almost always distinguishable clinically from gonoblennorrhea. In extensive bacteriological studies, he was able to eliminate the conjunctival bacteria as possible etiologic agents, but concludes that bacterial infection may complicate the disease. The inclusions, he believes, are reaction products of the epithelial cells to a filtrable virus. He was unable to determine the exact etiology.

#### An Experimental Study

**Materials.** All cases of conjunctivitis occurring in infants born at the University Hospital over a period of 15 months have been available for this study. I am indebted to Dr. E. D. Plass, head of the Department of Obstetrics and Gynecology, and to his associates for their cooperation.

A total of 77 cases of conjunctivitis has been subjected to bacteriological study with the following findings:

Staphylococcus aureus (hemolytic) .....	41
D. pneumoniae .....	13
H. influenzae .....	5
D. pneumoniae and Staph. aureus .....	4
E. coli .....	1
Lacrimal conjunctivitis	
D. pneumoniae .....	1
D. pneumoniae and H. influenzae .....	1
Bacteriologically negative .....	11

It is interesting to note that no cases of gonococcal infection occurred in the

hospital series, a fact illustrating the value of the Credé method of prophylaxis.

The conjunctivitis due to known conjunctival bacteria, with the exception of the lacrimal cases, responded rapidly to treatment such as ½-percent silver-nitrate ointment, 1-percent optochin, or 1-percent mercurochrome. The total duration of these cases was in no instances longer than one week.

The eleven cases in which negative bacteriological findings were obtained constituted a distinct group characterized by (1) onset from five to nine days after birth; (2) resistance to silver nitrate or any other form of treatment; (3) long duration; (4) presence of basophilic heterogeneous inclusion bodies in the cytoplasm of certain of the epithelial cells.

**Clinical characteristics of inclusion blennorrhea.** The disease began acutely or subacutely from the fifth to the ninth day after birth. In general, the acute cases developed earlier than the subacute ones. Secretion was often profuse and in three of the eleven cases the early symptoms were suggestive of gonococcal infection. The acute phase of the disease was characterized by severe inflammation, edema, and infiltration of the conjunctiva, particularly marked in the fornices and in the lower tarsal area. The upper tarsal conjunctiva did not participate strongly in the inflammation. The picture was that of a severe papillary conjunctivitis. After a period varying from one to three weeks the acute stage was succeeded by a chronic stage of long duration (five months to one year or longer). During this time the inflammation and infiltration gradually regressed.

No gross corneal changes were observed but the frequent finding of a transient superficial punctate keratitis in adult cases suggested that if slitlamp examination had been possible some of the cases might have shown minor epithelial lesions. No pannus developed.

The prognosis of the disease would seem to be good. One case was clinically normal five months and a second case fourteen months after onset of the disease. The remaining ten cases still show



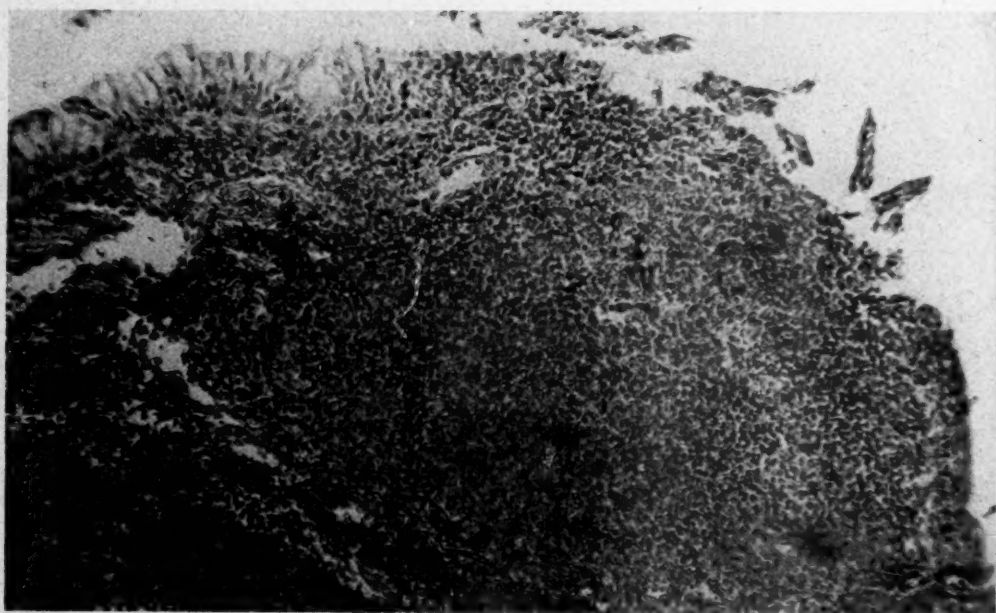


Fig. 1 (Thygeson). Section from upper fornix in case 7, forty-three days after onset of symptoms.

Fig. 2 (Thygeson). Section from upper fornix of a *Macacus rhesus* infected by transfer from a case of inclusion blennorrhoea.

activity at the end of observation periods varying from three weeks to eight months, but a return to an approximately normal condition is anticipated in all. Mild scarring has been reported by Lindner and more recently by Lumbroso<sup>11</sup>, but no cicatricial changes have occurred so far in my cases.

The frequent association of a persistent rhinitis has been noted by many observers. Such a rhinitis appeared in my second case and lasted about six weeks.

**Pathology.** A biopsy from the upper fornix was made in a single case on the 43d day of the disease. Sections revealed a dense subepithelial infiltration with inflammatory cells (fig. 1), plasma cells being in greatest numbers. There was no follicle formation. The epithelium was infiltrated with polymorphonuclear cells and in the superficial layers an occasional cytoplasmic inclusion body was seen.

All authors have stressed the lack of follicle formation in inclusion blennorrhea. Lumbroso<sup>11</sup>, however, has recently presented evidence to show that late in the disease (425th day) follicles may form. He also notes the presence of a mild, diffuse, subconjunctival fibrous-tissue development.

Follicle formation, however, is characteristic of the adult disease experimentally or accidentally acquired by transfer of conjunctival scrapings or secretions. Likewise the transfer to monkeys always produces a follicular conjunctivitis.

**Bacteriology.** All but one of the eleven cases of inclusion blennorrhea were subjected to intensive bacteriological study. In general, the plan was the same as that previously followed in bacteriological studies of trachoma<sup>21</sup>. Cultures were taken every second day during the entire period of hospitalization. Blood agar was the medium of choice, but supplementary cultures were made on Noguchi's semisolid leptospira medium, ascitic fluid blood agar, chocolate agar, Loeffler's blood-serum medium, and Noguchi's medium for the

cultivation of *Treponema pallidum*. Both aerobic and anaerobic methods were utilized. Material for culture was obtained by scraping the affected conjunctiva with a platinum spatula or loop. Occasionally the secretion alone, without epithelial cells, obtained by means of sterile cotton applicators, was used. Incubation was at 37°C. and at 30°C.

Air contaminants were eliminated, insofar as possible, by subjecting uninoculated tubes and plates to the same manipulations as the inoculated ones. It was thus possible to eliminate from consideration a number of air bacteria which otherwise might have caused confusion. The fact that Lumbroso<sup>11</sup> did not similarly control his studies probably accounts for a part at least of his rather bizarre bacteriological findings.

The results of bacteriological studies are indicated in table 1. It will be seen that in no case was the disease complicated by superimposed bacterial infection. Late in the disease, however, two cases showed small numbers of pneumococci. Their saprophytic role was indicated by the fact that there was no exacerbation of the symptoms coincident with their appearance, and further by the fact that they were not bile soluble (until virulence had been restored by mouse passage).

While no actual mixed infection occurred, the curious finding of a bacterial infection in one eye and an inclusion infection in the other was noted in the following two instances:

Case 7. A bilateral conjunctivitis was noted on the ninth day. Smears from the right eye revealed many gram-positive cocci in clumps. Smears from the left eye showed no bacteria but a moderate number of epithelial inclusions. Cultures from the right eye grew *Staphylococcus aureus* (hemolytic) while cultures from the left eye remained sterile. Treatment with ½-percent silver-nitrate ointment, three times daily, was begun in the two eyes. The left eye was unaffected by it but the right eye recovered rapidly and in five

Table 1

## BACTERIOLOGICAL FINDINGS IN INCLUSION BLENNORRHEA

Case	No. of Examinations	Results
1. G.	0	No bacteria seen in smears.
2. R.	5	Many colonies <i>C. xerosis</i> . Few <i>Staph. albus</i> .
3. B.	30	<i>C. xerosis</i> . <i>Staph. albus</i> . <i>D. pneumoniae</i> found 6 wks. after onset of disease.
4. K.	4	<i>C. xerosis</i> .
5. F.	28	<i>C. xerosis</i> , <i>C. hoffmani</i> , <i>Staph. albus</i> .
6. A.	5	<i>C. xerosis</i> .
7. S.	26	<i>C. xerosis</i> . <i>Staph. albus</i> . <i>D. pneumoniae</i> found 46 days after onset of disease.
8. H.	12	<i>C. xerosis</i> . <i>Staph. albus</i> .
9. W.	3	<i>Staph. albus</i> .
10. M.	8	Many colonies <i>C. xerosis</i> . <i>Staph. albus</i> .
11. H.	2	<i>C. xerosis</i> .

days had returned to normal. Seven days later the right eye became acutely involved. Cultures were negative but epithelial scrapings revealed numerous inclusions. It was evident that a transfer infection from the left eye had occurred.

Case 10. A bilateral conjunctivitis developed on the eighth day. Smears from the right eye showed many gram-positive cocci in clumps; smears from the left eye showed no bacteria but many inclusions. Under treatment with silver-nitrate ointment the right eye cleared rapidly while the left eye remained unchanged. When the infant was taken from the hospital on the fifteenth day the right eye was approximately normal.

**Transmission experiments.** *Ordinary laboratory animals.* Seven attempts to transfer the disease to the conjunctivae of white rabbits were unsuccessful. Four similar attempts each with the guinea-pig, white rat, and dog also failed. Epithelial scrapings from active cases induced no inflammatory changes when inoculated into the anterior chamber of the rabbit's eye or intraperitoneally in the rat.

*Monkeys.* Ten *Macacus rhesus* were inoculated. These animals proved rather difficult to infect, direct transfer from

early acute cases being required. If the material was diluted or allowed to stand for intervals of fifteen minutes or longer, no disease resulted. Six infections were produced, however. The disease was a chronic follicular conjunctivitis, involving the fornices but leaving the upper tarsal conjunctiva relatively unaffected. It resembled strikingly the conjunctivitis produced by fresh strains of *Bacterium granulosis*<sup>22</sup>. In fact, a clinical differentiation between the conjunctivitis in the *M. rhesus* induced by direct inoculation from trachoma or inclusion blennorrhoea and that induced by cultures of *Bacterium granulosis* does not appear possible. The pathological picture, as illustrated by figure 2, is also similar to or identical with that produced by the other two agents. The conjunctivitis lasted from two to three months and healed without gross scarring. Transfer to the uninoculated eye occurred in two cases.

In a single Sooty Mangabey a follicular conjunctivitis with more striking inflammatory signs developed. Here, again, the upper tarsus participated but mildly in the inflammation, whereas the remainder of the conjunctiva was hyperemic and infiltrated. During the first ten days there was a moderate amount of secretion.



Two sphinx baboons developed a type of follicular conjunctivitis more comparable to that seen in the human eye. The disease resembled mild cases of the follicular type of swimming-bath conjunctivitis. Follicles were most pronounced on the lower lid but were also well developed in the upper fornix. The upper tarsal conjunctiva was hyperemic and infiltrated but showed no follicle formation. Secretion was considerable during the first two weeks of the infection.

The baboon appears to be the logical experimental animal since it is sensitive to infection yet is not prohibitive in price. The *Macacus rhesus*, while cheap, is too resistant.

*Man.* Two human volunteers with blind eyes were available for inoculation. Both were elderly individuals with normal conjunctivae.

Experiment 1. Scrapings from the upper culdesac of a patient with an active case of inclusion blennorrhoea were divided into two portions, one for bacteriological study, the other for inoculation. The latter portion was applied to the conjunctiva of the right eye after gentle scarification. No change in the eye was noted until the morning of the seventh day, when the lids were glued together by secretion and there was moderate conjunctival congestion. The inflammation increased until the tenth day after inoculation when it began to regress. The bulbar conjunctiva was only slightly hyperemic, the conjunctiva of the lower lid being involved predominantly. The picture was that of a diffuse papillary conjunctivitis. No follicular development was noticed at any time during the disease. The symptoms gradually abated, with complete return to normal by the ninetieth day. There was no corneal involvement and the left eye did not become affected.

Inclusion bodies were moderately abundant from the first day of the disease throughout an observation period of three weeks. There were no pathogenic bacteria. Cultures of the original material revealed only *C. xerosis*. Inoculation of my own eye with this bacterium did not induce disease.

Experiment 2. Inoculation in this case was made in a manner similar to

that in Experiment 1. Inflammatory symptoms also began on the seventh day. There was moderately abundant secretion during the first two weeks, followed by a gradual diminution in quantity. Bulbar injection was marked during the first week. The conjunctiva of the fornices was thickened and the general appearance was that of a severe papillary conjunctivitis. No follicles were seen at any time. On the fourteenth day of the disease the other eye became subacutely involved and followed the same clinical course as the first eye. Healing of both eyes was complete at the end of the fourth month. There were no corneal complications.

Culture of the material used for inoculation revealed only *C. xerosis* and *Staphylococcus albus*. Neither bacterium proved pathogenic when used for inoculation of my own eye. Cultures taken from the experimental disease at intervals during the first two weeks yielded only small numbers of the conjunctival saprophytes.

**Microscopic Findings.** *Secretion preparations.* In secretion smears from the acute stage of inclusion blennorrhoea, stained by Gram's method (1-percent safranin counterstain), no bacteria were ordinarily to be found. An exception to this must be noted in two cases in which moderate numbers of *C. xerosis* were seen and recovered in culture. In no one of the eleven cases, however, were the conjunctival pathogens found. When the secretion smears were stained with Giemsa and passed through two changes of 95-percent alcohol (about 5 seconds in each), to decolorize the neutrophilic granules, an entirely different picture was seen. Free and included in the leucocytes were many minute, sharply defined granules, the elementary bodies, which stained reddish blue with Giemsa. In addition there was a small number of larger coco-bacillary bodies, the initial bodies, which stained blue and bipolarly with Giemsa. All transition stages between these and the elementary bodies were present. The elementary and initial bodies are most numerous during the early and acute stage, but could be found in small numbers throughout most of the clinical course of the disease. Their number

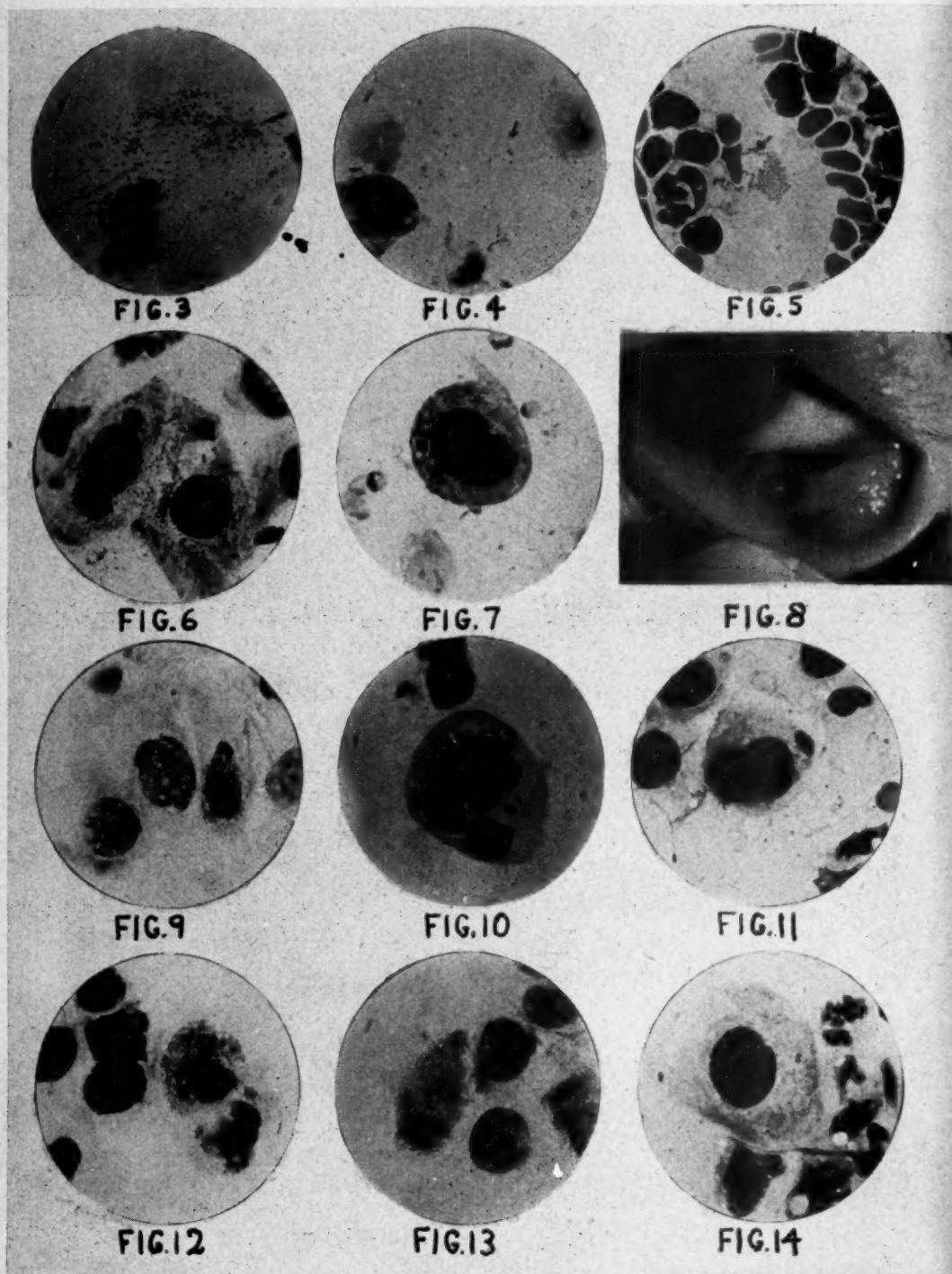


Fig. 3 (Thygeson). Free elementary bodies in secretion from a patient with inclusion blennorrhoea with acute onset.

Fig. 4 (Thygeson). Initial body in secretion from an acute case.

Fig. 5 (Thygeson). Large form of psittacosis virus. Mouse-spleen-impression smear, courtesy Dr. S. P. Bedson.



FIG. 15



FIG. 16

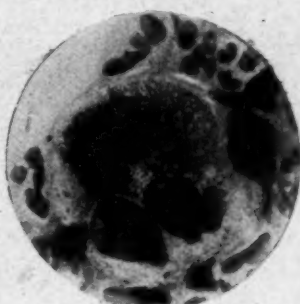


FIG. 17

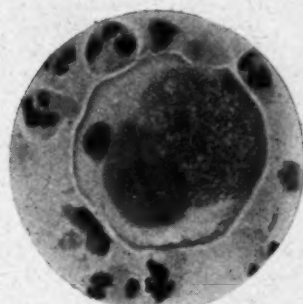


FIG. 18

Fig. 6 (Thygeson). Inclusion bodies from an experimental infection of the adult human eye.

Fig. 7 (Thygeson). Elementary-body inclusion from an experimental infection of the adult human eye.

Fig. 8 (Thygeson). Infection of my own left eye obtained by inoculation with a bacteria-free suspension of elementary bodies.

Fig. 9 (Thygeson). Initial-body inclusions from an experimental infection produced by inoculation with a bacteria-free suspension of elementary bodies.

Fig. 10 (Thygeson). Nine inclusions in a single epithelial cell.

Fig. 11 (Thygeson). Densely packed inclusion resembling the "morula" stage of the psittacosis virus colony. Vaginal smear from mother in case 9.

Fig. 12 (Thygeson). Elementary-body inclusion replacing the entire cytoplasm of the epithelial cell. The nucleus has undergone partial degeneration.

Fig. 13 (Thygeson). Elementary-body inclusion with degeneration of the cell nucleus.

Fig. 14 (Thygeson). Epithelial cell containing a single initial body.

Fig. 15 (Thygeson). Large inclusion made up of initial and elementary bodies. The initial bodies tend to lie at the periphery.

Fig. 16 (Thygeson). Elementary-body inclusion in vaginal smear from mother in case 10.

Fig. 17 (Thygeson). Large elementary-body inclusion in vaginal smear from mother in case 10.

Fig. 18 (Thygeson). Two inclusions in a large vaginal epithelial cell from mother in case 11.

varied quite constantly with the amount of secretion and in most cases was also in proportion to the degree of inflammation. It is well known, however, that individual persons vary greatly in their reactions to a single irritant or toxin,

which probably accounts for the fact that two negro babies showed severe inflammation without much secretion. In these two infants the loose tissue of the fornices, characteristic of negro babies, became very chemotic, thus



simulating a severe disease. The free bodies occurred in moderate numbers only, in each instance.

**Epithelial scrapings.** In preparations made from epithelial scrapings the picture was similar to that of the secretion preparations except that the free bodies were much more numerous. In addition, inclusion bodies were present in the cytoplasm of many of the epithelial cells.

**The morphology of the elementary bodies.** The elementary bodies (fig. 3) are minute granules of uniform size (about  $0.25\mu$  in average diameter) which stain reddish blue with Giemsa and poorly and slowly with ordinary aniline dyes. They are gram negative. The bodies closely resemble in size and staining reactions the minute elementary bodies characteristic of such filtrable virus diseases as vaccinia, fowl-pox, and psittacosis\*. They are readily differentiated from the neutrophilic granules, which they somewhat resemble in size, by the fact that they are alcohol fast while the neutrophilic granules decolorize rapidly. They are differentiated from the occasional nonspecific granules met with in smear preparations by their uniform size, frequent diplococcal form, and their peculiar reddish-blue color with Giemsa.

Phagocytosis of the elementary bodies by leucocytes is frequent but there is no evidence of their multiplication within these cells.

**The morphology of the initial bodies.** The initial bodies (fig. 4) are coccobacillary in shape and vary from  $0.3$  to  $0.8\mu$  in their greatest diameter. Like the elementary bodies they are gram negative and stain poorly with aniline dyes, a point differentiating them from the conjunctival bacteria. With Giemsa they stain blue and bipolarly. Division forms are frequent. In morphology and staining reactions they are identical with the initial bodies of trachoma and strikingly similar to the large form of psittacosis virus (fig. 5)<sup>24</sup>.

**Evidence that the elementary and initial bodies constitute the etiologic agent of the disease.** On the basis of the

following findings the elementary and initial bodies may be identified as the causal agents in inclusion blennorrhoea:

(1) *Constant presence in the disease.* In the eleven cases studied, these bodies were extremely numerous at the onset and diminished gradually with the clinical symptoms.

(2) *Absence in conjunctivitis of known bacterial origin.* Sixty-seven cases of conjunctivitis of the newborn caused by such bacterial agents as *N. gonorrhoeae*, *D. pneumoniae*, *E. coli*, *H. influenzae*, and *Staphylococcus aureus* were subjected to careful and repeated examination. In no case were elementary or initial bodies seen. Two hundred and sixty-five cases of bacterial conjunctivitis of the adult were similarly examined with the same result.

(3) *Absence of pathogenic bacteria in inclusion blennorrhoea and failure of the occasional saprophytes to produce the disease when used for inoculation.* With the exception of the occurrence of pneumococci late in the course of two cases, only the usual conjunctival saprophytes were recovered. All types of these were repeatedly used for inoculation of my own conjunctiva without result. The significance of the pneumococci has been already considered.

(4) *Multiplication of the elementary and initial body in the new host when the disease is transferred to the normal human conjunctiva.* Clear evidence of multiplication of the bodies was obtained in the two transfer infections to the human eye (figs. 6 and 7). As will be described later, multiplication begins immediately after inoculation and can be demonstrated during the incubation period of the disease.

(5) *Production of the disease with bacteria-free suspensions of elementary bodies.* It was possible in two instances to obtain typical infection of the adult human eye (fig. 8) by inoculation with pure elementary-body suspensions. Removal of bacteria was obtained by passage of the suspension through a colloidion membrane having an average pore diameter of  $0.7\mu$ . The elementary bodies are of such size\* that after saturating the adsorptive surfaces of the pores of the filter they pass through

\* I am indebted to Dr. S. P. Bedson of London, England, for psittacosis preparations.

\*  $0.25\mu$  average diameter when stained.

freely while bacteria, being considerably larger, are effectively retained.

Experiment 1. A bacteria-free filtrate obtained from a patient with an early and severe case of inclusion blennorrhea was used for the inoculation of an eye, blind from glaucoma. On the eighth day subacute inflammation and moderate secretion appeared. By the twelfth day a typical swimming-bath conjunctivitis, follicular type, had developed. The inflammatory symptoms and the secretion, which was never profuse, gradually diminished. The cornea remained normal. Only the usual conjunctival saprophytes were found in cultures taken daily from the eye over a period of ten days. Moderate numbers of inclusions (fig. 9) were found.

Experiment 2. My own left eye was inoculated by instillation of a few drops of a bacteria-free filtrate containing elementary bodies. On the morning of the sixth day there were secretion and moderate bulbar and palpebral conjunctival congestion. These symptoms increased until the tenth day when follicle formation began in the fornices. There was much bulbar congestion but little secretion.

At intervals there was slight transient superficial punctate keratitis involving the upper part of the cornea, associated with subjective symptoms of photophobia and irritation. There were moderate swelling and tenderness of the preauricular lymph node. The subsequent course was that of a swimming-bath conjunctivitis of the follicular type. No pathogenic bacteria were found on repeated cultural examinations. Inclusions were found in small numbers.

(6) *Filtrates not containing elementary bodies are not infective.* It was not possible to demonstrate elementary bodies in filtrates when collodion membranes of A.P.D. less than  $0.25\mu$  were employed. The fact that such filtrates were not infective (23 inoculations) indicates that the infectivity of filtrates is dependent upon the presence of elementary bodies and affords strong evidence of their etiologic significance.

**The inclusion bodies.** The inclusion bodies constitute intracellular colonies of elementary and initial bodies in various stages of development. The smallest

inclusions are made up entirely of initial bodies and the largest ones, which in the early stages of the disease may entirely replace the cytoplasm of the cell, are made up entirely of elementary bodies. All intermediate stages are observable. It is clear that an intracellular development from initial body to elementary body takes place. For descriptive purposes it is convenient to speak of the inclusions as initial-body type, mixed type, or elementary-body type, according to the stage of development.

The initial-body type (fig. 9) is composed of large coccoid or cocco-bacillary bodies, the initial bodies, which take a deep-blue stain with Giemsa. The individual morphology of the bodies is often lost when dry fixation is used, but a clear morphological picture is obtainable by the use of wet fixation. Typically the inclusion hugs the nucleus, often in the form of a sort of cap, but isolated inclusions are not rare. Multiple inclusions in a single epithelial cell occur frequently (fig. 10). Unlike the free initial body, the intracellular initial body does not always show the typical bipolar staining.

In inclusions of intermediate size there is evidence of multiplication of the initial bodies, which are smaller and often densely packed, forming a sort of "mulberry mass" (fig. 11). With wet preparations the mass is seen to be within a cytoplasmic vacuole. In spite of numerous references in the literature to a so-called plastin, no indications of such a substance were observed. In densely packed inclusions, individual morphology is often lost but the mass never loses its essential granularity.

In the largest inclusions (fig. 12) the fine granules (elementary bodies) may be clearly resolved. The inclusion now stains a reddish blue, somewhat difficult to recognize with low magnification but absolutely characteristic. While the early and intermediate types of inclusions, when few in number, may be confused by those unfamiliar with them with nonspecific bodies, such as extruded nuclear substance or phagocytosed nuclear debris, the elementary-body inclusion is absolutely typical and cannot be confused with artefacts nor any cytoplasmic structure.

The epithelial cells in most instances appear to tolerate the presence of the inclusions with little structural damage to the nucleus. Some cells, however, particularly in the early and acute phase of the disease, show extensive nuclear changes as illustrated in figs. 12 and 13.

*The life cycle.* All stages in the development of the inclusion from the initial-body to the elementary-body stage may be followed. So much of the life cycle is beyond argument. The remainder of the cycle is open to several interpretations. The one which seems most logical and probable to me and which coincides with the microscopic findings considers the elementary body to be the infective stage and is as follows: (1) A free elementary body penetrates an epithelial cell and because of the satisfactory nutrition obtainable, (2) develops into an initial body (fig. 14). (3) The initial body then divides, becoming progressively smaller in size until (4) the elementary-body stage (fig. 12) is reached. The cell is now weakened because of exhaustion of cytoplasmic substance and (5) ruptures either spontaneously or because of pressure occurring during the movement of the lids with consequent scattering of the elementary bodies into the secretion. This interpretation differs from that of Lindner<sup>23</sup> and of Howard<sup>25</sup> who have considered the initial-body stage the infective one. It is true that free initial bodies are seen in the secretion but their numbers are small as compared with the elementary bodies. It seems probable that the presence of free initial bodies may be accounted for by the occasional rupture of an inclusion in which development to the elementary-body stage has not been entirely completed. Such inclusions (fig. 15) are not uncommon. A strict parallel for my interpretation is seen in psittacosis in which Bedson<sup>24</sup> has demonstrated the elementary stage of the virus to be the infective one while the large form of the virus (corresponding to the initial body of inclusion blennorrhea) is of low virulence.

*Duration of the life cycle.* While inclusion blennorrhea is frequently unilateral at onset (six cases), transfer to the other eye has always occurred. In

case 10, this transfer was anticipated and was produced experimentally by deposition of a small amount of secretion from the affected eye on the tarsal conjunctiva of the normal eye. No scarification nor friction was employed. Scrapings taken prior to inoculation showed no inclusion bodies and the eye was clinically normal. Scrapings were then taken from the lower tarsal conjunctiva at definite intervals with the following results:

30 hours: Conjunctiva normal. Scrapings revealed numerous inclusions, 99 percent being of the elementary-body type, the remaining 1 percent being of mixed type. There were no leucocytes.

51 hours: Conjunctiva normal. Numerous inclusions, 99 percent being of early initial-body type. A few free elementary bodies and an occasional polymorphonuclear neutrophile.

75 hours: Conjunctiva normal. Numerous inclusions, mostly of mixed type, with an occasional elementary-body type.

100 hours: Conjunctiva normal. Numerous inclusions, mainly of elementary-body type. A few very early initial-body inclusions. Increased leucocytic reaction.

122 hours: Inflammation and secretion were beginning. Inclusions of initial to mixed type predominated. Many polymorphonuclear leucocytes.

144 hours: Inflammation and secretion marked. Mixed inclusions predominated. A few elementary-body inclusions. The cycle had now become somewhat indistinct.

165 hours: Majority of inclusions of elementary-body type with a few of the initial-body type.

Three complete cycles from elementary body to elementary body were thus observed during the first six days after inoculation. This finding suggests that the life cycle of inclusion-blennorrhea virus is approximately 48 hours. It is interesting that this figure agrees with that determined by Bedson<sup>24</sup> for the life cycle of psittacosis virus.



**Filtrability of virus of inclusion blennorrhea.** Like psittacosis virus, inclusion-blennorrhea virus filters only in the elementary-body phase. Filtrability is dependent upon the preparation of virulent suspensions of high elementary-body content, since it is necessary to have more than sufficient virus to saturate the adsorptive surfaces of the pores of the particular type of filter used. With kieselguhr filters such as the Berkefeld or Mandler, the adsorptive properties are a seriously complicating factor due to the necessarily extensive pore surfaces present in even the smallest models. The series of graded collodion membranes, developed by Elford<sup>26</sup>, are more nearly true filters since pore size and not adsorption is the more important factor in determining the size of the particle passed or retained. Using the Elford filters of average pore size greater than  $0.6\mu$  and filtration area of  $0.64$  sq. cm., it was possible consistently to pass elementary bodies when material from early acute cases was employed. It was not possible to produce virulent filtrates with material from the chronic stage of the disease owing to the limited material available and the scarcity of elementary bodies.

The high loss of virus which occurs even when collodion filters are employed can be demonstrated by comparing the elementary-body content of the filtered and unfiltered suspensions. When the elementary-body content is low, it is frequently necessary to centrifugalize the suspension (30 minutes at 18,000 R.P.M.) to concentrate the bodies for staining purposes. The high-speed centrifuge offers a satisfactory means of concentrating dilute elementary-body suspensions obtainable from chronic or subacute cases.

**Genital origin of inclusion blennorrhea\*.** The theory of the genital origin of inclusion blennorrhea is supported by the finding of typical inclusion bodies (figs. 16, 17, 18) and free virus in preparations from the vaginas of the four mothers so far examined. The in-

fectivity of the vaginal secretions in three of the cases was proved by transfer to the eyes of sphinx baboons, with the development in each case of a typical follicular conjunctivitis. Material in the fourth case was transferred to the eye of a *Macacus rhesus* which did not develop the disease.

Inclusion bodies were found in material from the cervix and from the vagina but not in scrapings from the urethral aperture. In one case the inclusions were numerous; in the other three cases they corresponded in number to those in a case of inclusion blennorrhea a month or more after infection. Free elementary bodies were numerous in the one case but few in number in the others.

In one of the cases there was a post-partum febrile reaction with temperatures reaching  $103^{\circ}$  F. There was profuse vaginal discharge in which hemolytic streptococci were found. In the other three cases the post-partum histories were normal. In no one of the four cases was a history of previous pelvic infection obtainable.

It seems obvious that inclusion infection of the female genito-urinary tract must be a mild disease. No clinical entity which could be due to an inclusion infection is recognized either by the urologist or gynecologist, although a large number of nonspecific infections of unknown etiology are encountered. There is, however, a type of nonspecific urethritis of the male in which bacteria are not found. The subacute symptoms disappear after a few weeks and the disease heals without complications.

**Relation of inclusion blennorrhea to swimming-bath conjunctivitis.** The four transfer infections from inclusion blennorrhea as well as the one accidental infection of the mother of the infant in case 1 all resulted in a clinical picture and course typical of the disease known as swimming-bath conjunctivitis. The identity of swimming-bath conjunctivitis and inclusion blennorrhea has been suggested by Löhlein<sup>5</sup> and Gebb<sup>10</sup> and recently by Morax<sup>27</sup>.

During the period of the present study, three cases of adult inclusion conjunctivitis, all in university stu-

\* I am indebted to Dr. L. J. Harris for the examination of patients and collection of materials used in these experiments.

dents, were observed in this clinic. All had the mild, follicular type of disease. One case, in a negro graduate student, was followed clinically and bacteriologically throughout the entire course of his illness, of which the following is a report:

G.M., aged 23 years, gave no history of swimming-pool infection. He presented himself one week after the onset of the illness complaining of inflammation, irritation, and slight secretion in the left eye. The right eye was normal. Examination of the left eye revealed a severe follicular conjunctivitis characterized by massive follicle formation in the fornices. The upper tarsal conjunctiva was hyperemic, infiltrated, and contained a few small follicles. There was moderate secretion. The cornea and limbus were normal to slitlamp examination. Cultures taken on varied media at each hospital visit grew only limited numbers of the usual conjunctival saprophytes. Conjunctival scrapings, stained with Giemsa, showed no bacteria, but revealed small numbers of free elementary and initial bodies as well as a moderate number of inclusion bodies. The inclusions diminished gradually in number until at the end of the sixth week of the disease they could no longer be found. They reappeared temporarily during a flare-up of the disease which occurred during the third month, then disappeared again. Free virus was demonstrable each time for some weeks after the inclusions had apparently disappeared. Healing of the disease without scarring or pannus now appears complete at the end of the sixth month.

**Types of swimming-bath conjunctivitis.** Two types of adult inclusion infection are known. The one, typified by the two direct-transfer inoculations, is a papillary conjunctivitis with subacute or acute inflammatory symptoms, considerable secretion, and fairly numerous inclusions. Follicles are either absent or are masked by the papillary hypertrophy. The second type is the most common and is exemplified by an accidental infection (mother of the infant in case 1) and by the two filtrate inoculations. Here the picture is of a

chronic follicular conjunctivitis without much secretion or inflammation. The inclusions are usually demonstrable only during the first few weeks of the disease and are few in number. It is readily understandable how the inclusions have been entirely missed in certain of these cases. The attempt made by Lindner<sup>28</sup> to separate swimming-bath conjunctivitis into two diseases, the one with inclusions and the other without, appears to be unjustified. I concur fully with Morax<sup>27</sup> in the opinion that swimming-bath conjunctivitis is a single clinical entity.

**The nonidentity of inclusion blennorrhea and trachoma.** According to Lindner<sup>28</sup> there are two types of trachoma: (1) the acute genital type which produces inclusion blennorrhea in the newborn and an acute trachoma in the adult; and (2) chronic trachoma produced by a virus which, though originally of genital origin, has been carried from eye to eye and has become chronic and stubborn in comparison with the disease of direct genital origin. Lindner's theory has been contested by many, however, and the results of my four experimental transfers to the adult, as well as of the accidental infection previously reported, fully confirm the findings of Gebb, Löhlein, Morax, and others who have sharply distinguished inclusion blennorrhea and swimming-bath conjunctivitis from trachoma.

### Discussion

An attempt has been made to identify the agents of psittacosis<sup>31</sup> and inclusion blennorrhea\* with the Rickettsiae. While certain similarities do exist between these agents and the Rickettsiae, such as staining reactions and intracellular mode of existence, the latter differ from the viruses, as Bedson<sup>32</sup> has pointed out, in the following respects: they never form inclusions, they produce filamentous forms, and they have an arthropod as one of their hosts. The name *Rickettsia psittaci*<sup>31</sup> as applied to the causal organism of psittacosis is

\* Two prominent virus workers who have examined my inclusion blennorrhea material have suggested that the agent should be classed with the Rickettsiae.

thus inappropriate and appears to be disappearing from the current literature.

Most virus inclusions are acidophilic and homogeneous, whereas the cytoplasmic masses of inclusion blennorrhea are basophilic and heterogeneous. It is apparent, however, that no strict definition of a virus inclusion can be formulated according to these specifications, since the inclusion of psittacosis is basophilic and homogeneous while the intranuclear inclusion of yellow fever is acidophilic and heterogeneous. Furthermore, the essential similarity of the inclusions of inclusion blennorrhea to those of such virus diseases as vaccinia, fowlpox, and molluscum contagiosum is well shown by the recent investigations of Goodpasture and Woodruff<sup>29</sup>, and Goodpasture, Woodruff, and Buddingh<sup>30</sup>. Their findings indicate that the acidophilic, apparently homogeneous inclusions of these diseases are in reality composed of myriads of minute granules, the elementary bodies, embedded in an amorphous acidophilic material, the matrix, which varies in composition in the different diseases. The identity of the elementary body and the virus has been demonstrated in vaccinia<sup>33, 34, 35</sup> and fowl-pox<sup>36</sup> and appears probable in molluscum contagiosum<sup>37</sup>. The view that the cytoplasmic inclusion bodies of many virus diseases are in reality intracellular virus colonies seems thus to have considerable experimental evidence to support it.

Virus workers in this country have been prone to eliminate from the group of virus diseases all those in which visible microorganisms are found, e.g., psittacosis, a practice which has probably resulted from the widespread belief that the viruses are nonliving, enzyme-like agents. The nonliving nature of the viruses, however, has never been proved, and the view that the viruses are minute living microorganisms seems to be gaining adherents rapidly. The elimination of inclusion blennorrhea from the group of virus diseases because of the size and obvious living nature of its causal agent would seem illogical. Since inclusion-blennorrhea

virus shares with other viruses the common properties of (1) filtrability, (2) cytotropism (inability to multiply in the absence of living cells), and (3) inclusion formation, it should be classed with other viruses of large-particle size, the best-known examples of which are the viruses of vaccinia, fowl-pox, molluscum contagiosum, and psittacosis.

#### Summary and Conclusions

1. Inclusion blennorrhea is a distinct clinical entity characterized by its time of onset (5 to 9 days after birth), by its long duration (3 months to 1 year), by its resistance to treatment, and by the presence of cytoplasmic inclusion bodies in certain of the conjunctival epithelial cells.

2. The etiologic agent of the disease is a filtrable virus having an elementary-body phase and an initial-body phase. Filtrability is dependent upon the elementary-body phase.

3. The inclusion bodies constitute intracellular colonies of the virus in various stages of development, the initial body being the early stage and the elementary body the late and infective stage. The cycle from elementary body to elementary body requires approximately 48 hours.

4. Filtrability of the disease is low, owing to the difficulty of obtaining virulent suspensions of sufficient elementary-body content to satisfy the adsorptive properties of kieselguhr or porcelain filters. With graded collodion membranes of average-pore size greater than 0.6  $\mu$ , however, it is consistently possible to prepare virulent filtrates from acute cases.

5. The virus is not cultivable on artificial media but requires living human or monkey epithelial cells for multiplication.

6. The resistance to treatment of inclusion blennorrhea is probably dependent on the inability of antiseptic solutions to reach the virus, which is intracellular during most of its existence.

7. Inclusion blennorrhea and swimming-bath conjunctivitis are caused by the same virus, the clinical differences in the two diseases being due to the difference in the reactivity of the con-



junctivae of the newborn and the adult.

8. All cases of inclusion blennorrhea and most cases of swimming-bath conjunctivitis are derived from a virus disease of the genito-urinary tract which is demonstrable by the finding of inclusion bodies and is transferable to the eyes of monkeys.

9. Both inclusion blennorrhea and swimming-bath conjunctivitis are entirely distinct from trachoma. The study of inclusion blennorrhea, however, paves the way for an understanding of the inclusions and the free elementary and initial bodies of trachoma.

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**Discussion.** DR. ALAN C. WOODS (Baltimore): Will this virus pass a Berkeley N filter?

DR. THYGESON: No, it will not.

DR. WOODS: In patients with this disease, is there a sensitivity to intracutaneous tests with filtrates?

DR. THYGESON: That is something yet to be tested.

DR. FREDERICK H. VERHOEFF (Boston): I was wondering if the inclusion virus he is dealing with ever occurs in the nuclei of epithelial cells. So many other inclusion bodies do.

DR. THYGESON: We occasionally see epithelial cells in which the nucleus is degenerated and the membrane broken. Then we see elementary bodies mixed in. But I don't believe in a living epithelial cell there is invasion. I haven't seen any.

CHAIRMAN CLAPP: Do I understand in swimming-pool conjunctivitis there are no infection bacteria?

DR. THYGESON: There is no bacterial infection primarily responsible for the disease. It is always possible to have secondary infection. In my cases, there has not been any.

CHAIRMAN CLAPP: Then there is no such thing as swimming-pool conjunctivitis?

DR. THYGESON: I think the name is a misnomer now because we don't see it often in swimmers. Inclusion conjunctivitis would be preferable. The source of infection has been argued a great deal and I think it is due to secretion from the genito-urinary tract. The mother in the last case had a profuse vaginal discharge. A case like that could contaminate a small body of water.

## STUDIES ON THE INFECTIVITY OF TRACHOMA

### I. The Transfer of a Conjunctival Infection to Monkeys by Means of Trachomatous Tissues

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The occurrence of follicles has been observed to follow the transfer of trachomatous material to the conjunctiva of monkeys. The experimental infection is preceded by an incubation period of several days to a month. The follicles frequently extend to the uninoculated eye. The infection persists for a few weeks to many months, but without exhibiting scar-tissue formation or corneal involvement. The histological changes accompanying the infection consist chiefly of follicles composed of small lymphocytes and plasma cells surrounded by a layer of fibroblasts.

Material obtained from human trachoma varies greatly in infectivity for monkeys. Thus of 62 tissues from active trachoma studied, only 41 were infectious. Similarly, there is a great variation in individual susceptibility of monkeys to infection, but it is felt that the resistance observed in certain animals is relative and not absolute.

The infectivity of a given tissue does not appear to be related to the presence or absence of epithelial inclusions in the tissue used for inoculation. Similarly, frequent examinations of infected monkeys failed to reveal the presence of inclusions.

Attempts to establish the disease permanently in monkeys by serial passage from animal to animal were unsuccessful. The infectious agent was usually lost by the third animal-to-animal transfer.

Recovery from the experimental disease did not affect the course nor character of later infection by the same agent. It has been possible to induce the disease 2 and 3 times successfully in the same animals, thus indicating a complete inability of the monkey to establish an immunity to the infection. On the other hand, recurrence of the disease was not stimulated by a variety of nonspecific agents. From the Bacteriological Laboratories of the Oscar Johnson Institute, Washington University, School of Medicine, Saint Louis, Missouri. The entire work was conducted under a grant from the Commonwealth Fund of New York City.

A precursory study of the literature on trachoma reveals immediately the confusion existing on the subject. Primarily due to a general vagueness of the cause\*, the confusion is magnified by

the frequent contradictions among different workers who have introduced several hypotheses to explain the evolution of the disease. While it seems that the balance of evidence should ac-

\* The recent isolation by Noguchi (Jour. Exp. Med., 1928, v. 48, Supplement No. 2) of Bact. granulosis in trachoma and his interpretation of its causal relationship to the disease has been confirmed by Olitsky and his coworkers (Rev. Trach. 1930, v. 7, p. 173;

Jour. Exp. Med., 1931, v. 54, p. 31). While this organism is the best candidate as cause of trachoma, it has not received universal acceptance and confirmation (Vide Bengtson, I. P., U. S. Public Health Rep. 1932, v. 47, p. 1914).

tually indicate that trachoma is a communicable disease, nevertheless this is not generally accepted, and instead several distinct and different concepts have been substituted to explain the etiology. Thus, to mention some of the more commonly advanced theories, certain investigators<sup>1</sup> believe that defective or deficient diet plays the dominant part in trachoma. Others<sup>2</sup> reason that it represents a local manifestation of a generalized disease, while particularly the Italian School<sup>3</sup> consider it basically dependent upon an altered lymphatic constitution. The suggestion has also been made that trachoma is an expression of an allergic state, possibly to various pollens<sup>4</sup>. Even among those who regard the disease as a specific infection there is disagreement respecting the nature of the causative organism. That the organism concerned is a filterable virus<sup>5</sup>, a bacterium<sup>6</sup>, a fungus<sup>7</sup>, protozoan<sup>8</sup>, or even the "inclusion"<sup>9</sup> seen in the epithelial cells of the conjunctiva has not received general consent. Indeed, the opinion<sup>10</sup> is expressed even, that trachoma is induced by repeated infection by one or more varieties of bacteria, thus signaling the disease as a non-specific infection.

In the face of all this confusion, it is obvious that in undertaking an intensive study of the etiology of trachoma, it becomes necessary to establish first of all certain fundamental conditions regarding the character of the disease; and this naturally requires a repetition in part or *in toto* of experiments already described in the literature. In order, then, to construct the proper background for this study, observations have been made on the infectivity of trachoma and its transmissibility to animals. Some of the data have been published in a preliminary communication<sup>11</sup>, but a detailed and complete report of this study is being made at the present time.

### Methods

**Material.** Material for study was obtained from the U. S. Trachoma Hospitals at Rolla, Missouri, and Richmond, Kentucky, and from the Indian

School at Fort Defiance, Arizona\*\*. All the patients were selected with great care on the basis of typical conjunctival and corneal signs. Most of the patients were untreated but even when treatment had been given, it was mild enough not to have interfered with the results to be described. The trachoma in most instances was of recent date, and uncomplicated by secondary infection, as judged by clinical examination and bacteriological cultures. The material was obtained either by swabbing or grattage. In the latter instance, the conjunctival scrapings were collected under novocaine anesthesia from all four lids in 1.5 c.c. sterile salt solution.

**Inoculations.** Inoculations were made by swabbing or injection. Swabbing was performed either directly from the patient's eye to the animal or by immersing the swab in the container with grattage material and then rubbing gently the surface of the everted lid. Injections were made with ground scrapings by multiple pricking of the surface of the conjunctiva, allowing material from the syringe to run over the scarified area, and then introducing the tissues subconjunctivally. In some instances the quantities for injection varied but in general, 0.2 c.c. of the material was adopted. A 26-gauge needle was used for scarification and injection. Early in the study, one upper lid only of the animal was inoculated, but later both upper lids were inoculated.

### Experimental

Preliminary experiments were conducted on the ability of trachomatous material to infect a number of animals. Inoculations were made either in the conjunctiva or by different routes in rabbits, guinea pigs, rats, and dogs. All these animals proved to be refractory to infection. Consequently, the work to be reported was conducted entirely on monkeys, with the bulk of the study on *M. rhesus*.

\*\* For the kind cooperation in furnishing patients and extending the facilities of the respective hospitals, appreciation and indebtedness is expressed to Drs. C. E. Rice and J. E. Smith (Missouri), Robert Sory (Kentucky), and Paul D. Mossman (Arizona).



1. **Infectivity in monkeys of trachomatous material.** That whole conjunctival material from patients with trachoma is infectious for monkeys was established early in the course of the study, and this fact already has been reported upon by a number of workers<sup>12</sup>. In this study it was found that infection may be transmitted to monkeys equally well, whether the inoculation is made by simple swabbing or injection as described above and the resulting infection shows no variations in severity or character dependent upon the manner of transfer. It should be noted, however, that

ly the bulbar conjunctiva. Shortly after the first appearance of follicles in the upper lid, they develop also in the lower lid, usually in the center of the cul-de-sac.

Extension of the infection to the uninoculated eye occurs fairly regularly in periods varying from one to four weeks after follicles have appeared in the first eye. As is brought out in table 1, of 22 monkeys infected in one eye, the infection spontaneously extended to the uninoculated eye in 14, or in more than half the animals. The onset, course, and character of the infection is similar in both eyes. It is not possible to state, however, how much of the infection in the uninoculated eye is actually extension and how much represents possible manual transfer of the infection by the monkey.

At the height of infection, the follicles are characterized by uneven distribution, variability in size, and marked vascularization, which, in certain instances gives the follicles a blood-red color. At no time during the experimental disease is the papillary form of trachoma observed, so that the infection is typified by a folliculosis only.

The duration of infection varies considerably in different animals. While follicles may completely disappear within a few weeks, they may persist indefinitely in some animals, so that up to the present time several monkeys have had a continued infection for more than two years. In general, however, the follicles regress completely in considerably more than half the animals within a period of six months (cf. table 2). Eventually, moreover, the animals recover spontaneously without showing any sign in the conjunctiva of a past infection. At no time has the infection been observed to extend beyond the conjunctiva; the cornea remains clear and unvascularized throughout the course of infection, thus failing to exhibit one of the most dominant clinical signs.

Occasionally, tissue was removed for pathological examination\*. The his-

\* The writers wish to thank Dr. H. D. Lamb for making the pathological examinations.

Table 1

EXTENSION OF FOLLICLES FROM INOCULATED TO UNINOCULATED EYE

Number of monkeys infected in one eye	Number of monkeys with extension to uninoculated eye
22	14

attempts to infect monkeys by introduction of trachomatous material into tissues other than the conjunctiva were completely and uniformly negative, thus exemplifying an agent with an exquisitely developed capacity for selection and localization. The incubation period in successfully infected animals varies in different individuals, so that if the appearance of follicles be accepted as the first tangible sign of infection, then it may be stated that the incubation period varies from 5 days to 3 or 4 weeks (vide table 2). In this study, however, the incubation period was not greater than two weeks in considerably more than half the animals infected.

Within a few days following inoculation, the conjunctiva exhibits a definite thickening, with mild inflammation and injection but with usually no increased secretion or exudate. The follicles first begin to appear near the inner canthus, and within a few days at the external canthus. Usually, follicles then form a ridge, progressing from both angles and meeting in the center of the retrotarsal fold. Eventually, the follicles reach deep into the cul-de-sac, only occasionally covering the tarsus and even more rare-

tological changes were more or less similar in infected animals and the variation encountered in different individuals was one of severity only. The follicles were of varying size and vascularity;

because, while characteristic, they are not differential in early trachoma and other clinically similar conjunctivitis.

A great variation occurs in the infectivity of tissues from different patients.

Table 2

## INFECTIVITY OF TRACHOMATOUS TISSUES FOR MONKEYS

Number of monkeys infected	Incubation period in weeks				Duration of follicles in months								
	1	2	3	4	2	4	6	8	10	12	16	20	24
65	*22	20	18	5	+12	22	12	3	5	3	1	0	2

\* These figures represent the number of animals. +One of the 12 given in this list recovered in about one month.

The total number of animals listed under duration of follicles is less than the total number infected. This discrepancy is explainable by the fact that both conjunctivae were excised in some of the animals at the height of the disease for purposes of serial passage. It was therefore impossible to include these animals in this part of the protocol; in other animals one conjunctiva was removed, so that observations were continued in the opposite eye.

when large, they pushed outwards the surface epithelium, indirectly causing an interspersation of invaginations. The follicles were composed of small lymphocytes and plasma cells surrounded by a thin collar of fibroblasts, which sometimes showed bizarre-shaped nuclei. Usually, the covering was stratified, columnar epithelium exhibiting a marked degree of mucoid degeneration. Scar tissue was only rarely observed

Despite the fact that care was exercised in selecting persons in whom the trachoma was of comparatively recent onset, had been diagnosed as active, and in whom no treatment or only a minimum of treatment had been applied, half the patients from whom material was studied proved to be inactive or noninfectious for monkeys. As shown in table 3, of 82 patients studied, material from only 41 proved to be in-

Table 3

VARIATION IN INFECTIVITY OF TRACHOMATOUS TISSUE AND IN SUSCEPTIBILITY OF *M. rhesus* TO INFECTION

Number of Tissues		Number of inoculations	Number of Monkeys				
Studied	Inactive		Infected after				Not infected
			1st	2d	3d	4th	
			Inoculation				
82	41	157*	35	17	11	2	38**

\* Each inoculation was considered as of a different animal, so that this number is greater than the actual number of individual animals studied.

\*\* It was not possible to continue successive inoculations until infection occurred, since some of the animals died and others were used for different experiments. In any case, these animals were inoculated with trachomatous material at least once, and the majority, twice.

and then in small quantities, but it was never clear whether this was the result of the infection or of the manipulation incident to the injection. The histological changes are not particularly stressed

fectious. Obviously it has not been possible to predict the infectivity of a given material from the clinical condition of the patient. While there is no strict parallelism between infectivity and clin-

ical condition, in general it may be said that the earlier the disease, the more infectious the material.

Other workers have considered that the variation in individual susceptibility of monkeys determines the infectivity of a material. It has been observed in this study that the most refractory of animals may be infected eventually, provided a sufficiently potent material is used for inoculation. Thus it will be seen in table 3 that of 103 monkeys inoculated, 35 were infected following a single inoculation; in 17, two inoculations were made before infection occurred, in 11, three inoculations, and in 2, four inoculations. The interval between inoculations varied considerably, so that the infection cannot be interpreted as the result of repeated inoculations as such. The remaining 38 were not infected, but for unavoidable reasons it was not possible to inoculate them more than twice, and some were inoculated only once with trachomatous tissue. It should be pointed out in this connection, however, that infectious material is not of equal potency in different animals. Consequently, a tissue may infect only a certain proportion of a given group, indicating in another way the variation in resistance of different monkeys. It has been from a combination of figures of this type that table 3 has been devised.

That the infection in some of the above monkeys was not the result of repeated inoculations was determined by the observations made in three experiments. In each of the experiments four animals were inoculated once a week with trachomatous material, one group receiving 6, another 7, and the third 8 inoculations. The results obtained revealed no essential difference in either frequency, character, or duration of infection from those observed following one or more inoculations repeated irregularly, as indicated in table 3.

**2. The frequency of "inclusion" bodies in infectious material.** The basophilic, heterogeneous, rodlike structures observed in the cytoplasm of epithelial cells scraped from the conjunctiva in trachoma have been assumed by a num-

ber of workers to be either the actual incitant of trachoma or very intimately associated with the causative agent. While the evidence for this opinion is purely circumstantial and unconvincing, it has not been possible to exclude the "inclusion" body as of more than accidental occurrence. It seemed desirable, therefore, to study the possibility that the infectivity of a tissue might be related to the presence of "inclusion" bodies. Accordingly, 50 consecutive specimens were examined for the presence of inclusions together with their ability to infect monkeys. A summary of this study is given in table 4. It is

Table 4

RELATION OF INFECTIVITY OF TRACHOMATOUS TISSUES TO THE PRESENCE OF "INCLUSION" BODIES

Number of Tissues Studied	Number Infectious	Number Not Infectious
(a) With "inclusions" 26	12	14
(b) Without "inclusions" 24	10	14

seen that of 26 tissues containing "inclusions," 12 were infectious for monkeys, while 14 were not. Of 24 tissues lacking "inclusions," 10 were capable of infecting monkeys, the remaining 14 having no effect on the animals. It is of further significance that of the 14 animals not infected following inoculation with tissues containing "inclusions," a sufficient number were subsequently infected with active material, some containing and some lacking "inclusions," thus indicating that failure of infection on the first attempt was not due to an extraordinary degree of resistance. It seems logical to conclude, therefore, that the infectivity of a trachomatous tissue does not depend upon the presence or absence of "inclusion" bodies.

This conclusion obtains confirmatory evidence from observations made in monkeys. While it has not been possible to make a detailed, periodic examination of scrapings from infected animals for "inclusion" bodies, since this causes a relatively rapid retrogression and disappearance of follicles, sufficient obser-



vations have, nevertheless, been made at irregular intervals over varying periods of time. On no occasion, have epithelial-cell "inclusions" ever been seen in scrapings made from monkeys infected with trachomatous material.

**3. Serial passage of infection in monkeys.** The desirability of establishing the infection in monkeys by successive transfer from animal to animal requires little explanation. The problem of eti-

jected consisted of the excised tarsus and retrotarsal conjunctiva removed at the height of the infection under general ether anesthesia. The tissues were then ground and injected into normal animals as described above. The results of these experiments reveal that only 13 of 37 monkeys inoculated were infected. The tendency toward a prolonged incubation period was consistently observed. The infection was mild,

Table 5

SERIAL PASSAGE OF TRACHOMATOUS INFECTION IN MONKEYS

Experiment	Number of Monkeys			Incubation Period	Severity	Duration
	Furnishing Tissues	Inoculated	Infected		of Infection	
1	4	4 by swabbing 7 successive days	3	2-3 weeks 1-5 weeks	mild	1-died after 5 weeks 2-2½ months
2	2	2 by swabbing and injection*	0			
3	2	2 by injection	0			
4	3	6 by swabbing	2	1-3 weeks 1-4 weeks	mild	about 1 month
5	2	6 by injection	3	1-3 weeks 2-4 weeks	mild	about 1 month
6	2	4 by injection	2	2 weeks	mild	1-3 weeks 1-1 month
7	4	8 by injection	0			
8	1	3 by swabbing	2	4 weeks	mild	about 1 month

\* For purposes of injection, material was obtained from infected animals by excising both tarsus and retrotarsal tissue under general ether anesthesia. The tissues were then emulsified by grinding and subsequently inoculated as indicated.

ology of trachoma might be facilitated in this way by supplying an adequate source of infectious material, and by increasing the virulence of the causative agent and thus perhaps rendering its ultimate isolation more possible. A number of such experiments were carried out and the more typical are summarized in table 5. In these 8 experiments, the animals furnishing the material were heavily infected, and material from them was transferred to 37 monkeys. Except in 3 instances (experiments 2, 3, and 8), inoculations were made by injection. The material in-

jected consisted of the excised tarsus and retrotarsal conjunctiva removed at the height of the infection under general ether anesthesia. The tissues were then ground and injected into normal animals as described above. The results of these experiments reveal that only 13 of 37 monkeys inoculated were infected. The tendency toward a prolonged incubation period was consistently observed. The infection was mild,

Several other experiments were undertaken to study a third serial passage. The results were discouraging. Most of the animals showed no development of follicles at all, and the rare monkeys with follicles showed only a few which disappeared in a matter of weeks.

It was realized, therefore, that trachomatous infection is not permanently adaptable to monkeys, and that by the third animal passage the infectious agent is usually completely dissipated.

**4. Resistance following partial or complete recovery from infection.** One of the characteristic features of clinical trachoma is the lack of immunity to re-

ly or partially from the experimental infection were inoculated with active material from humans. The numerous difficulties in conducting such an experiment should be pointed out. The period of time consumed is great, with the result that some of the animals are lost by death. Trachomatous material is not obtained with regularity, and when it is obtained it is impossible to predict its degree of activity. Consequently, the interval between recovery and reinfection is frequently undesirably prolonged. Nevertheless, 17 animals were inoculated upon complete recovery with successful reinfection. In 2

Table 6

COMPARISON IN 10 TYPICAL MONKEYS<sup>+</sup> OF FIRST AND SECOND INFECTIONS, BOTH INDUCED BY TRACHOMATOUS TISSUE

Monkey	First Infection			Second Infection			Interval between infections
	Inoculation	Incubation	Duration	Inoculation	Incubation	Duration	
1-8	Injection	6 days	10 weeks	Injection	18 days	12 weeks	10 weeks
1-9	Injection	21 days	11 weeks	Injection	6 days	7 weeks	2 weeks
1-10	Injection	22 days	1 year	Swab	17 days	*14 weeks	3 weeks
1-11	Injection	8 days	13 weeks	Swab	17 days	*14 weeks	8 months
2-17	Swab	8 days	12 weeks	Swab	7 days	20 weeks	1 week
2-20	Swab	21 days	11 weeks	Injection	7 days	18 weeks	1 week
3-21	Swab	21 days	7 weeks	Swab	17 days	*14 weeks	10 weeks
3-22	Injection	10 days	8 weeks	Swab	10 days	13 weeks	2 weeks
3-23	Injection	6 days	9 weeks	Injection	7 days	14 weeks	1 week
3-24	Injection	6 days	9 weeks	Swab	7 days	9 weeks	5 months

<sup>+</sup> 17 similar experiments were done and 2 animals were infected successfully 3 consecutive times, as described in the text.

\* In these animals, the conjunctivae were removed for serial passage, so that observations could not be recorded beyond the periods indicated.

infection. While in many instances exacerbation of the clinical symptoms in an arrested infection is probably due to the continuous but latent presence of the agent in the conjunctiva, it is, nevertheless, of equal likelihood that recurrence of trachoma is the result of reinfection. With a large number of animals recovering from the experimental disease, an opportunity was afforded to study the response of monkeys to successive infections. In the meantime, careful observation of recovered animals during the past three years has never revealed spontaneous recurrence of the disease.

For the purpose of this experiment, animals which had recovered complete-

ly, in fact, it was possible to cause infection a third time. A typical protocol of 10 animals is presented in table 6. It is obvious that in spite of the frequent variations in the individual animal in incubation period, duration of lesions and intervals between infections, the conclusion is warranted that reinfection occurs with similar frequency, similar character and duration to that observed in the first infection. These results coincide with those obtained by Hetler in a similar study<sup>15</sup>. In the two animals suffering a third infection, the course and character of the disease was of the same order as the first. It is, therefore, apparent that partial or complete recovery from succes-

sive infections induced by inoculation of trachomatous material affords an animal neither increased susceptibility nor increased resistance to this disease.

It is axiomatic of clinical trachoma that various intercurrent conditions cause an exacerbation or return of symptoms. Whether this is an example of nonspecific stimulation or merely an alteration of the tissues that allows the agent temporarily in abeyance to flamminate again is not clear. It was, nevertheless, interesting to determine whether a similar state occurs during the experimental infection. Numerous attempts have been made to induce a nonspecific response in partially or completely recovered animals. Amongst the various methods used have been injections of different cultures, filtrates of trachomatous tissues, material from human folliculosis, treatment with chemicals, and mechanical irritation. It has not been possible, however, to cause a recurrence of any of the symptoms of the experimental disease by any of the nonspecific agents mentioned.

### Discussion

That an infection may be transmitted to apes and monkeys by transfer of trachomatous material had been demonstrated by a number of observers. In this respect, this study has confirmed their results. It has been shown in this report that material obtained by grating or simple swabbing of the human trachomatous conjunctiva contains an agent capable of infecting the conjunctiva of *M. rhesus*. The human material, however, is not infectious for other animals commonly employed in the laboratory study of disease, and it is tolerated without effect even by monkeys when introduced in tissues other than the conjunctiva.

The infection induced in the conjunctiva is preceded by a varying incubation period which averages, however, from 10 to 14 days. The disease is manifested by the appearance of follicles which are transient, lasting from weeks to months, and, in rarer instances, to years. The follicles eventually retrogress completely and leave no permanent changes in the lid, without ap-

parently recurring spontaneously. The cornea, moreover, does not participate in the infection.

The material from human trachoma exhibits great differences in its infectivity in monkeys. The patients selected for study were chosen with the expectation from the clinical history and symptoms that their tissues would be infectious. Nevertheless, only half of the tissues were actually capable of transmitting infection to monkeys. It has not been possible, therefore, to predict the infectivity of a given material, although, despite numerous exceptions, the earlier the infection, the more infectious the material. On the other hand, the animals also possess a marked variation in susceptibility. Even when active material is employed, a number of monkeys may fail to become infected, thereby necessitating successive inoculations, until a particularly potent specimen is used.

That the infectivity is not related to the presence or absence of epithelial-cell "inclusions" is amply brought out by the data. Infections have been induced in monkeys with equal success by employing material either containing or lacking "inclusions." Moreover, frequent examinations of conjunctival scrapings have invariably failed to reveal the presence of "inclusions" in infected animals. It is difficult, therefore, to reconcile these observations with the concept that "inclusions" are intimately involved in the etiology of trachoma.

It has not been possible to establish the experimental disease permanently in monkeys. Serial passage of the infection from animal to animal indicates that the incubation is retarded, the symptoms are milder, and the duration of the lesions is diminished. Usually, the agent is lost by the third animal transfer, thus indicating the high specificity of the infectious agent of trachoma for human tissue. It is interesting, in this connection, to point out experiments conducted by Hetler and James<sup>14</sup> in this laboratory concerning the influence of diet on the conjunctival infection in monkeys. Their data disclose that in animals suffering vitamin-A deficiency, the disease transferred



with trachomatous material differs from the infection in normal animals in the following respects: a longer incubation period, less involvement of the lids, lack of extension from one eye to the other, and shorter duration of the follicles.

Recovery from the experimental disease does not affect the course and character of subsequent infection by the same agent. The data indicate that second and third reinfections behave in a manner similar to that of the primary infection. Attempts to induce nonspecifically recurrence of the disease in recovered animals failed with the agents employed. In other words, there is no immunity to the experimental infection and reinfection occurs only when the specific agent is applied *de novo*.

### Summary and Conclusions

1. Material derived from the conjunctiva of patients with trachoma contains an agent capable of inducing infection in the conjunctiva of monkeys.

2. The infection is preceded by an incubation period varying from several days to a month, when follicles appear over the surface of the conjunctiva and

frequently extend to the uninoculated eye.

3. The follicles regress in a few weeks to many months, without cicatrization.

4. The cornea never participates in the infection.

5. The histological changes accompanying the infection consist chiefly of follicles composed of small lymphocytes and plasma cells surrounded by a layer of fibroblasts.

6. Tissues from different patients show a great variation in infectivity.

7. Individual monkeys exhibit marked differences in resistance to infection.

8. The infectivity of a given tissue is apparently independent of the presence or absence of so-called "inclusion" bodies.

9. Efforts by serial passage have failed to adapt permanently the infectious agent in monkeys.

10. No increased susceptibility or resistance to reinfection has been observed in any of the animals completely or partially recovered from the experimental disease.

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## THE SIGNIFICANCE OF THE REPTILIAN "SPECTACLE"

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The "spectacle" of snakes and certain lizards is homologous with some portion of the palpebral complex, though perhaps not the same portion in all cases. It is surely protective against mechanical injury to the cornea, but Rochon-Duvigneaud's theory that it is an inevitable consequence of the crawling habit is not accepted. The only spectacled diurnal lizards are those exposed to wind-driven sand. All other spectacled reptiles are either subterranean or combine a close-crawling habit with a nocturnality either present (Gekkonidae, Xantusiidae, Pygopodidae) or demonstrable for their ancestors (snakes). Unspectacled nocturnal forms (*Heloderma*, *Sphenodon*, crocodiles) are all large bodied and carry their eyes well out of the dangers which beset those of geckoes, etc. The presence of the spectacle is thus correlated, in most cases, not simply with crawling but with crawling and nocturnality. Diurnal crawling forms can see and avoid injurious objects on the ground and have had no need for a spectacle.

Shielding the eyes of certain fishes and of many reptiles and replacing, in the latter, a mobile palpebral system, is a transparent cap which has been called the "spectacle" (lunette, Brille, of foreign writers). This motionless window is leathery in the fishes, dry and horny in the reptiles. In the snakes it is responsible for the animals' "glassy stare," and its outer layer is shed periodically along with the stratum corneum of the integument.

These structures have long been known and have been variously accounted for both as to their homologies and their value to their possessors. Rochon-Duvigneaud<sup>1</sup> has shown that in Teleost fishes the spectacle is a delamination-product of the cornea<sup>2</sup>, and has firmly established the palpebral nature of the analogous structure in the snakes. Whether in the latter the spectacle has been derived from the nictitating membrane (as the prominence of the Harderian gland suggests) or, as Rochon-Duvigneaud inclines to think, from either the lower lid alone or from both upper and lower lids, are matters on which there is as yet no embryological data<sup>3</sup>. Again, the homologies of rep-

tilian spectacles must probably be determined separately for the snakes and for each of the five whole families of lizards (and scattered representatives of still other families) which bear them.

The ocular caps of reptiles are now unanimously dismissed as "protective" against mechanical injury to the cornea, though some other notions have been held in the past. We shall concern ourselves here with a more intimate inquiry into the significance of the reptilian structure. While the "protection" theory is clearly accurate as far as it goes, it does not at all account for the sporadic distribution of the spectacle within the reptilian group. The reptiles which have produced a spectacle, either permanent and perfect or temporary and incomplete (in the form of a transparent window in a mobile lower lid) fall into three groups:

A. *Deserticolous lizards*: the genera *Ophiops*, *Ablepharus*, *Cabrita*, *Eremias*, *Chalcides*, and many others mentioned in the standard works on reptilian natural history. The first two named, as their very names indicate, have as perfect spectacles as the snakes; the others have the mobile "window."

<sup>1</sup> Rochon-Duvigneaud, A. La protection de la cornée chez les vertébrés qui rampent (serpents et poissons anguiformes). Ann. d'Ocul., 1916, v. 153, pp. 185-202.

<sup>2</sup> The situation in the lampreys, which he includes in his explanation of the Teleost spectacle, is more probably to be interpreted as a primitive condition in which the head skin has not yet formed the conjunctiva fixa and corneal epithelium seen in the higher vertebrates. In other words, it is probable that in these most primitive of living vertebrates the future conjunctiva has not yet become conjoined, and that the window which occurs in the head skin is thus primary and not secondary.

<sup>3</sup> Since the above was written, the extensive work of H. Schwarz-Karsten has come to the writer's attention (Über Entwicklung und Bau der Brille bei Ophidiern und Lacertiliern und die Anatomie ihrer Tränenwege. Morphol. Jahrb., v. 72, pp. 499-540). This author finds that the ophidian spectacle arises from the upper and lower lids, chiefly the latter.



B. *Subterranean lizards*: the families Aniellidae and Amphisbaenidae, with reduced eyes bearing permanent spectacles.

C. *Miscellaneous forms*: all snakes, and the three lizard families Gekkonidae, Xantusiidae, and Pygopodidae; all with permanent protection.

Rochon-Duvigneaud, whose treatment of the present topic is the most elaborate, has correlated the presence of the spectacle with the habit of crawling, and has ignored the many nonreptant fishes which are far from "anguiform," and the many lizards, both limbed and limbless, ambulatory and reptant, which possess such structures. Nor has he accounted for the absence of the spectacle in many lizards which are as truly reptatory as any snake, trailing the limbs and wriggling their way through vegetation; nor for the lack of this structure in such very snakelike forms as *Anguis fragilis* and our American "glass snake," *Ophisaurus ventralis*, whose mobile lids and visible tympanic membrane are their only obvious lacertilian characteristics.

Rochon-Duvigneaud restricts his discussion to the serpents and the fishes, and considers the permanent protection offered by the spectacle to be a vital necessity to the snakes, since he believes them to be guided wholly by vision, a moot point in the light of Baumann's demonstration<sup>4</sup> of the olfactory powers of serpents. It is also an open question whether it is, after all, fatal even for an animal which is wholly dependent upon vision, to have to blink periodically. The cause of *Anguis* alone is sufficient to show that the crawling habit, as such, does not demand the presence of a spectacle.

We approach, then, the task of accounting for the spectacle with grave

doubts as to the universal applicability of Rochon-Duvigneaud's interpretation even for terrestrial vertebrates<sup>5</sup>. These doubts serving to open our minds, we are free to agree with the herpetologists that the temporary and permanent spectacles in the members of our group "A" (v.s.) are protective against sharp, wind-blown sand particles. Similarly, the legless, burrowing forms in group "B" have produced a spectacle, not because they are reptant, but because they force their heads through soil which would enter even tightly closed lids.

For our heterogeneous group "C," there seems at first thought no possible inclusive explanation. Here are lumped all snakes, whose "walks" of life may be on or under the soil, in fresh or salt water, among rocks, in trees—there is even one snake that flies<sup>6</sup>. Here also are the Geckoes<sup>7</sup> and their close imitators but distant relatives, the Night Lizard *Xantusia* and its tropical allies; and the Australian leaf-footed lizards—the snakelike Pygopodidae. None of these lacertilian families is entirely deserticolous or entirely subterranean, and only the last named is entirely "reptile" in Rochon-Duvigneaud's sense.

The various lizards in group "C" inhabit all possible types of terrain, and in fact run the entire gamut of habitats occupied by the various unspectacled lizards with the exception of water—none of the group "C" forms is aquatic. There are thus no obvious environmental factors operative with them, as with groups "A" and "B," to encourage a tendency to spectacle formation. Falling back upon efforts to find important biological features which the animals themselves have in common, we meet with a double success: all of the lizards in group "C" are nocturnal, and all are either so small or so angui-

<sup>4</sup> Baumann, F. Experimente über den Geruchssinn der Viper. Rev. Suisse Zool., 1927, v. 34, pp. 173-184.

<sup>5</sup> The spectacled fishes include some, like *Cobitis*, which burrow in sand; others, like *Protopterus*, which aestivate in a desiccated condition; and a large number, such as the mud-skipper and the eels, which have the habit of leaving the water for extended periods of time. The need for protection of the cornea against drying seems to have been responsible for most piscine spectacles (see Plate, L. Allgemeine Zoologie und Abstammungslehre, 1924, Teil 2, Jena, Fischer).

<sup>6</sup> The East Indian *Chrysophelea ornata*.

<sup>7</sup> A very few delicate, slow-moving members, some of which, such as *Coleonyx*, have strongly serrated, mobile lids.

form that, like the snakes, they are forced to put their corneae in jeopardy from sharp, rough objects—gravel, stubble, bark, and the like.

Thus our tentative explanation is that the geckoes, night lizards, and leaf-footed lizards have produced spectacles not simply because they "reptate," but because they are small and are active in dim light, where harmful objects easily avoided by their diurnal, pure-cone, foveate lacertilian relatives—however "reptile"—become doubly, trebly dangerous.

Two apparent difficulties stand in the way of making this tentative conclusion conclusive and permanent:

1. Most modern snakes (and one or two genera of spectacled geckoes) are diurnal; but in another place I have shown that the snakes had their inception as a nocturnal, or at least photophobic, group<sup>8</sup>. Though the central family of serpents (the Colubridae) adopted diurnality, the mobile lids of their remote ancestors, once lost, could not be regained; for that is an immutable law of evolution. Thus, far from its being a structure of great virtue for them, as

Rochon-Duvigneaud maintains, the majority of snakes carry a spectacle for which they have no further need.

2. Some nocturnal reptiles lack spectacles; but these are the massive, non-reptant crocodiles and their allies, the "living fossil" *Sphenodon*<sup>9</sup>, and the slug-gish, egg-eating Gila monster, *Heterodermus*. All of these are large bodied—much larger than any of the group "C" lizards—and thus are capable of holding the head well above all rigid perforatives.

It is, then, our conclusion that the reptilian "spectacle," except where produced in partial or perfect form as a protection against wind-blown sand, or to facilitate digging, has been evolved as a consequence of nocturnal creeping, present or past. The small, close-crawling reptiles of the past, venturing out by night, had to pull up their lower lids, or pull over their nictitating membranes, as the bird in flight is said by some to do. Their invention of the spectacle has relieved their descendants of this inconvenience.

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<sup>8</sup> Walls, G. L., and Judd, H. D. The intra-ocular colour-filters of vertebrates. Brit. Jour. Ophth., 1933, v. 17, pp. 641-675 and 705-725.

<sup>9</sup> Which to be sure inhabits a burrow; but the burrow is preëmpted, and the animal has not at all the same protection problem as *Aniella*.

## THE INFLUENCE OF DIETARY DEFICIENCY ON THE TRANSMISSIBILITY OF TRACHOMA TO MONKEYS

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The influence of dietary deficiency on the transmissibility of trachoma to monkeys was studied. Twenty-two malnourished monkeys were inoculated with fresh trachomatous material; follicular changes developed in the inoculated eyes in seventeen monkeys after a period of 16-37 days and persisted for 17-90 days. There was no transfer of the process to the uninoculated eye. In 15 well-nourished monkeys inoculated by the same technic, follicular changes developed in 13 after a period of 8-30 days, spread to the uninoculated eye, and persisted for 5-10 months. Neither macroscopic scarring of the conjunctiva nor corneal involvement occurred in either series. Diets low in vitamins, low in protein, and high in fats were used. From the Oscar Johnson Institute, Washington University, School of Medicine, Saint Louis, Missouri. Conducted under a grant from the Commonwealth Fund of New York.

While a number of opinions exist regarding the etiology of trachoma, some writers suggest that vitamin deficiency may be a factor predisposing or contributing to the onset and character of this disease. Thus Stucky<sup>1</sup>, in 1926, proposed that trachoma is primarily a deficiency disease. He reported both curative results in treatment and the prevention of relapses by utilizing foods rich in vitamin A as an adjunct to local treatment. At about the same time Royer<sup>2</sup> also suggested the possibility that trachoma might be a dietary-deficiency disease. Madden<sup>3</sup>, in 1928, and Sutton<sup>4</sup> and Gibson<sup>5</sup>, in 1931, suggested that dietary deficiency is necessary to the establishment of the disease and contributes to its persistence. Rice and coworkers<sup>6</sup> in the past few years have failed to produce any improvement in the trachomatous lesions in patients fed for a short period of time on an adequate diet reinforced with vitamins A, D, B, and G. Tilden and Miller<sup>7</sup> and Kendall and Gifford<sup>8</sup> conducted studies of this problem on an experimental basis. Tilden and Miller, in 1929, attempted to infect vitamin-A depleted monkeys with *Bacterium granulosis*, and Kendall and Gifford, in 1930, attempted to infect vitamin-A depleted rats with *Bacterium granulosis* and with material from human trachomatous lesions. In neither study, however, was it possible to draw any conclusions, for follicles did not develop in the inoculated eyes of either the well fed or

the malnourished animals. It is obvious, therefore, that the question of the influence of dietary deficiency on the transmissibility of trachoma to monkeys has not been answered conclusively. It seemed desirable to re-study the problem and, if possible, to obtain more convincing data. Accordingly, an attempt was made in our laboratory to infect the eyes of malnourished and of well-fed monkeys with material from human trachomatous lesions. Observations are presented here to show the response of normal and of malnourished monkeys to infection with material from trachomatous eyes.

### Experimental

Monkeys, rats, rabbits, and guinea pigs were used as experimental animals. They were fed adequate or inadequate diets. The deficient diets were low either in vitamin A or in protein. Diets high in fat were also given. The adequate diets contained all the known food requirements. Positive results were obtained only with the monkeys and therefore most of this report will be devoted to the results obtained in the eyes of the monkeys.

Trachomatous material was secured from patients both in the outpatient clinic of the Washington University School of Medicine and in the U. S. Trachoma Hospital at Rolla, Missouri\*; In other instances, it was secured from the infected conjunctiva of monkeys. The material was obtained

\* We are indebted to Dr. C. E. Rice and coworkers for material from the Rolla Hospital.



by rubbing a sterile swab over the conjunctival surface of the upper and lower lids or by grattage. Inoculations were made by swabbing the conjunctiva of the experimental animals.

A description of the eye condition of some of the patients from whom trachomatous material was taken is given in table 1. These patients showed undoubted trachoma and while typical of the trachoma patients from whom material was secured, form only a part of them. Material taken from those de-

of vitamin-A-free casein, egg white, crisco, sugar, cornstarch, oats. Osborne-Mendel salt mixture, and sodium chloride, contributing 13 percent protein, 60 percent carbohydrate, and 27 percent fat calories. The diet was adequate in all respects except vitamin A and was readily eaten by the monkeys. Although only 14 animals survived longer than six months on this food, one of these monkeys lived for 13 months and at that time showed all the typical symptoms of vitamin-A depletion.\*\*

Table 1  
SOURCES OF MATERIAL

No.	Age	Sex	Duration of Disease	Condition of			Vision		Infectivity for Monkeys
				Conjunctiva	Cornea	Lids	O.D.	O.S.	
1	16 yrs.	M	2 months	Acute papillary hypertrophy	Pannus upper $\frac{1}{2}$ O.U.	Normal position	20/20	20/20	Positive
2	6 yrs.	M	15 months	Acute follicular	Pannus upper $\frac{1}{2}$ O.U.	Ectropion lower lid	20/40	20/40	Positive
3*	18 yrs.	M	24 months	Follicular chronic scarred	Entirely vascularized	Ptosis	3/200	20/15	Positive
4	28 yrs.	M	24 months	Follicular chronic scarred	Pannus covering pupil O.U.	Entropion	20/200	20/200	Positive
5	48 yrs.	M	22 years	Smooth, scarred conjunctiva O.U.	Nebula O.U.	Entropion, Trichiasis	20/200	20/200	Negative

\* Left eye normal.

scribed in table 1 was used to inoculate the vitamin-A depleted animals and some of the control animals. The trachomatous material taken from the eyes of four of the five patients described proved to be infectious for some of the monkeys.

**I. Studies with animals on a diet low in vitamin A.** During the two-year period of the investigation, 27 monkeys were fed a diet low in vitamin A.\* The diet, Diet I, included tomato serum, viosterol, and a baked cookie consisting

At intervals during the depletion period the conjunctiva of the right eye of the 14 animals was inoculated with trachomatous material. In ten of the animals, as table 2 shows, follicles appeared in 17 to 35 days after the inoculation, were usually abundant, but pale, translucent, and never heavily vascularized. The conjunctiva usually became thickened and occasionally injected, but for the most part it was pale in the deficient animals. The follicles persisted in the infected eye for short

\* Full description of the technic and care of the animals will be published in The Journal of Nutrition.

\*\* Full description of the pathology of this animal will be published in The Journal of Nutrition.

Table 2

SHOWING THE EFFECT OF TRANSFER OF HUMAN TRACHOMATOUS MATERIAL TO THE CONJUNCTIVA OF MALNOURISHED AND OF CONTROL WELL-FED MONKEYS

Diet	Number of Monkeys Used	Eye or Eyes Inoculated	Number of Inoculations Resulting in Follicles	Time after Last Inoculation before Follicles Appeared. Days	Duration of Follicles		Character of Follicles	Character of Conjunctiva	Spread of Follicles to Untreated Eye
I Low in vitamin A.	14	O.D.	10**	17, 18, 18, 18, 22, 22, 22, 22, 30 <sup>o</sup> , 37	No. of Monkeys	Duration	Abundant, pale, translucent.	Pale until follicles appeared and then periodically became somewhat injected.	Never
II Diet I plus a source of vitamin A.	6	O.D.	5*	18, 18, 22, 30 <sup>o</sup> , 30 <sup>o</sup>	one for 1 wk. <sup>ooo</sup> one for 17 days one for 1 mo. six for 2 mos. one for 3 mos.	two for 5 mos. one for 6 mos. one for 8 mos. one for 10 mos.	Abundant, some were pale and translucent, many were inflamed.	Injected in all but one animal.	In every case after one to two months
III Low in protein.	4	O.D. and O.S.	3	16, 18, 20	Follicles were still present after 1 mo. <sup>ooo</sup> .		Not so abundant. Pale, translucent.	Pale in all but one animal.	Both eyes inoculated.
IV Low in protein and high in fat.	4	O.D. and O.S.	4	16, 20, 20, 24	Follicles were still present after 6 wks. <sup>ooo</sup> .		Abundant, pale, translucent.	Pale.	Both eyes inoculated.
V High in fat.	5	O.D. and O.S. in all but one monkey.	4*	16, 18, 20, 20, 24	Follicles present after one <sup>ooo</sup> to 6 months.		Abundant, pale, and translucent. Some were inflamed.	Pale in 2 animals; somewhat injected in others.	Both eyes treated in 3 monkeys. Second eye infected in two mos. in 4th animal.
VI Dog biscuit plus tomato toes.	2	O.D. and O.S.	2	8, 15	Follicles still present after 7 weeks. <sup>ooo</sup> .		Not so abundant but inflamed. Some were translucent.	Somewhat injected.	Both eyes inoculated.
VII Dog biscuit plus tomato toes, plus green leaves.	2	O.D. and O.S.	2	8, 17	Follicles still present after 7 weeks. <sup>ooo</sup> .		Abundant and inflamed. Some were pale and translucent.	Somewhat injected.	Both eyes inoculated.

Diets II, V, VI and VII are adequate in all known factors.

\* There were two animals on Diet I, two on Diet II, and one on Diet V which showed negative results after repeated inoculations. Finally transfer was made from an infected monkey to an uninfected monkey by saline swab. In 18 days in these five cases follicles appeared in the treated eye.

<sup>o</sup> Due to absence from the laboratory, inspection of these three animals was impossible until 30 days after the inoculations were made.

<sup>ooo</sup> Animal died.

<sup>ooo</sup> Observations discontinued.

\*\* Of the four monkeys showing negative results, three died within one to three weeks after the inoculations had been made.

periods of time, usually lasting only from three weeks to three months. There were no follicles in the uninoculated eye. The following descriptions give the typical sequence of reactions in two of these monkeys:

The right eye of monkey 120 was inoculated with human trachomatous material after the monkey had been eating the vitamin-A-low diet for four months. The eye was clear until 32 days after inoculation, when there was a thickening of the conjunctiva over the tarsal and retrotarsal regions. Tiny areas were elevated but there were no distinct follicles. Five days later, or 37 days after the inoculation, the retrotarsal area was injected and there were many distinct translucent follicles. The lids of the right eye became thickened, and more follicles appeared until the tarsal conjunctiva of both the upper and lower lids was involved. The cornea remained clear and the left eye was not involved. Three months after the appearance of follicles, the conjunctiva was again normal. Attempts to reinfect the eye with material from human trachomatous lesions were made during the remainder of the animal's life, but without success.

Monkey 111 remained in fairly good health on the vitamin-A-low diet for ten months. After the first two months on the diet, inoculation with trachomatous material led to a negative result except that there was a temporary thickening of the conjunctiva. Again, after six months on the diet, the right eye was inoculated, but again with a negative result. Finally, after eight months on the diet, inoculation of the right eye resulted in a positive reaction. One month after the inoculation, there were numerous large follicles and the conjunctiva was injected. Both lids of the right eye were involved, but the tarsus and the cornea of the right eye and the left eye remained normal. Seventeen days after the height of the reaction, the lids were entirely free from follicles.

The eyelids of rabbits, guinea-pigs, and of young and adult albino rats on the vitamin-A-deficient diet and on a complete diet were also treated repeat-

edly with some of the same material which was used to infect the monkeys. After such treatment the conjunctiva of these animals remained essentially normal.

**II. Studies with monkeys on an adequate diet.** Six monkeys fed Diet II, which consisted of Diet I, the diet low in vitamin A, with an added source of vitamin A, either tomato pulp or cod-liver oil, or both, made one group of controls. The conjunctiva of the right eye of these animals was inoculated at various times throughout the study whenever a depleted animal and suitable trachoma material were available. In the conjunctiva of all but one of these animals, as table 2 shows, follicles appeared in 18 to 30 days and persisted for periods of five to ten months, or longer. Many of the follicles on the conjunctiva of these animals had a beefy appearance due to their marked vascularization. Some of the follicles were pale and translucent. In every monkey, the infection spread to the uninoculated eye in one to two months after follicles appeared in the inoculated eye. Here, too, many of the follicles were heavily vascularized. The conjunctiva was injected in all but one animal.

**III. Studies with monkeys fed a diet adequate in all respects except protein.** Eight monkeys were fed Diet III, consisting of canned tomatoes, viosterol, and a baked cookie made of oats, wheat flour, sugar, cornstarch, Osborne-Mendel salt mixture, sodium chloride, lard, and egg white, contributing 8 percent protein, 22 percent fat, and 70 percent carbohydrate calories. This diet was inadequate as to both quantity and quality of the protein. Four of the animals thus fed died within a few weeks but at autopsy worms were found in the lymph nodes. The remaining four animals were given the low-protein diet for six months. They maintained a fairly constant weight, but looked malnourished and shaggy. Inoculations of the conjunctiva of both eyes were made with human trachomatous material after three to four months on the diet. Repeated inoculations were made in both eyes of these monkeys before follicles finally appeared in the lids of



three of the animals. The follicles, as table 2 indicates, occurred about three weeks after the inoculation. They were not very abundant and were translucent. The conjunctiva was pale. Autopsy and blood study of these animals revealed no abnormalities.

**IV. Studies with monkeys fed a diet furnishing low, inadequate protein and high fat.** Eight monkeys were fed Diet IV, consisting of canned tomatoes, cod-liver oil, and a baked cookie made of oats, wheat flour, sugar, cornstarch, Osborne-Mendel salt mixture, sodium chloride, lard, and egg white, contributing 8 percent protein, 52 percent fat, and 40 percent carbohydrate calories. Two animals in this group died, showing worms in the lymph nodes. Four of the six remaining animals maintained a fairly constant weight for six months but their fur became thin, shaggy, and greasy. They were emaciated but active, and always had good appetites. Two animals that had previously been fed a vitamin-A-low diet showed severe edema and died after four months on this low-protein, high-fat diet. After repeated inoculations of the conjunctiva of both eyes of the four remaining monkeys with human trachomatous material, finally, as table 2 shows, there appeared in the lids numerous small, translucent follicles. The conjunctiva was pale. Autopsy and blood study of these animals revealed no abnormalities.

**V. Studies with monkeys receiving an adequate diet supplying a high percentage of fat calories.** Six monkeys were fed a diet consisting of canned tomatoes, cod-liver oil, and a baked cookie made of casein, oats, sugar, Osborne-Mendel salt mixture, sodium chloride, lard, and egg white, contributing 15 percent protein, 50 percent fat, and 35 percent carbohydrate calories. The animals on this diet gained weight slowly and, with one exception, remained in a healthy condition throughout the period of observation. One of them, which had previously been fed the vitamin-A-low diet, lost weight on this high-fat diet. Inoculation of the conjunctiva of these animals resulted in follicles, as table 1 shows, in one or both

eyes in 16 to 24 days after the inoculation. Both eyes were inoculated in all but one of these animals, and in this animal the infection spread to the uninoculated eye two months after it had appeared in the inoculated eye. Some of the follicles in this group of animals were heavily vascularized. The nutritive condition of these monkeys was essentially normal.

**VI. Studies with monkeys on a complete and fully adequate diet.** In addition to the control group of monkeys reported in Section II, four monkeys on other normal diets were studied, in order to test fully the susceptibility of well-fed animals to the development, severity, and persistence of the infection. A diet consisting of Purina dog chow and whole tomatoes was fed to two monkeys. Eight to 15 days after inoculation with trachomatous material, numerous heavily vascularized follicles and a severe conjunctival reaction appeared in both eyes. Two other monkeys were fed Purina dog chow, whole tomatoes, and leafy vegetables. Again, as table 2 shows, follicles appeared in both eyes in eight to 17 days after inoculation. The conjunctiva was injected and the follicles were abundant and heavily vascularized. The follicles still persisted when the study was discontinued. Julianelle and Harrison<sup>9</sup> report persistence of follicles for a period of a year or longer.

#### Discussion

Although many transfers of trachomatous material to the conjunctiva of monkeys' eyes have produced no effects, it has again been shown that an infection may be transmitted from human trachomatous lesions, depending upon the infectivity of the material used and the susceptibility of the experimental animal. The nutritive condition of the monkey and particularly the normal vascular condition of the conjunctiva influence the severity of the infectious reaction. As Julianelle and Harrison<sup>9</sup>, as well as ourselves, have shown, the normal well-fed monkey responds with a positive reaction in from one to three weeks after the inoculation. Numerous pale and heavily vascular-

ized follicles appear, which usually persist for a period of from two months to a year or longer. The conjunctiva becomes thickened and injected. If only one eye of the monkey is inoculated, the infection occurs first in the inoculated conjunctiva and then extends to the other eye. The cornea is never involved. When the follicles disappear, there are no permanent changes in the lid.

When malnourished monkeys are used for similar inoculation, infection occurs in the inoculated eye almost as regularly as it does in the eye of a normal, well-fed monkey, although the incubation period is more prolonged. In

ring. Monkeys receiving inadequate protein also develop pale conjunctivae, which, in the few animals studied, were found to be difficult to infect. Of this group of animals, those on the low-protein and high-fat diet responded with a more severe reaction than those on inadequate-protein and lower-fat calories. The number of animals studied was too small for any definite conclusions to be drawn, other than that the response to infection with trachomatous material of these low-protein-fed animals is much less severe than it is in normal, well-fed monkeys. With a diet adequate in protein but high

Table 3

SUMMARY SHOWING EFFECT OF TRANSFER OF TRACHOMATOUS MATERIAL TO THE CONJUNCTIVA OF MALNOURISHED AND NORMAL MONKEYS

Condition of Monkey when Inoculated	Number of Monkeys Used	Number of Monkeys Showing Follicles	Character of Follicles	Character of Conjunctiva	Spread of Follicles to Uninoculated Eye†	Period between Inoculation and Appearance of Follicles	Duration of Follicles
Malnourished	22	17*	Pale	Usually pale	Never	16-37 days	17 days to 3 months
Normal	15	13	Inflamed and pale	Usually injected	Always	8-30 days	5-10 months

\* Three of the malnourished monkeys died within one to three weeks after the inoculation was made.

† In 14 of the malnourished animals only one eye was inoculated. In seven of the normal animals only one eye was inoculated.

the malnourished animal, particularly the vitamin-A-depleted monkey, the conjunctiva is pale, and the follicles which appear are pale and translucent rather than heavily vascularized. It is not unlikely, however, that this difference in appearance of the follicles is due to an anemic condition in the animal rather than to a decreased ability of the infectious agent to implant itself in the conjunctiva of the malnourished animals. The conjunctiva, at the height of the reaction, usually shows some thickening and injection, but soon becomes pale. There is no spread of the infection to the uninoculated eye. Follicles persist in the infected eye for periods of two weeks to three months and disappear without evidence of scar-

in fat calories, the monkeys are essentially normal, and respond to inoculations in about the same manner as noted in the control groups. Table 3 gives a summary of the data, showing the reactions manifested by the malnourished and the normal monkeys inoculated with trachomatous material. From these data, one may conclude that a malnourished monkey reacts less severely to inoculations of active material from human trachomatous lesions than does a well-nourished animal. A malnourished condition in a monkey apparently does not predispose to the development of the disease following inoculation with fresh trachomatous material.

Although the results here reported

with malnourished monkeys are very definite, one hesitates to interpret these findings in terms of human nutrition and trachoma. In the first place, the lesions occurring in the eyelids of the monkeys are not the same as those seen in human trachoma; in the second place, the material used for the inoculations can not be standardized and controlled; in the third place, there are no well-established standards for nutrition work with monkeys; and in the fourth place, there is still lacking any carefully controlled nutrition work with patients suffering from trachoma. Most of the patients seen by the writers seemed to be taking a fairly adequate diet and did not appear malnourished, but no intensive study was made of their physical condition nor of their dietary habits. The trachoma patients seen by us were very unlike the individuals described by Stucky<sup>10</sup> in his last review of his findings in Kentucky, but it is possible that there may be in the diets of individuals suffering from trachoma a hidden food lack which has contributed in the causation and persistence of the disease.

### Summary

The conjunctiva of normal, well-fed and of malnourished monkeys, rabbits, rats, and guinea pigs was treated with fresh trachomatous material obtained by swabbing and by grattage. A conjunctivitis characterized by follicular changes occurred in the monkeys, but not in the other animals. In the adequately nourished monkeys, the infection appeared within eight to 30 days, spreading to the uninoculated eye, and persisting from five to 10 months or longer, in both eyes. In the malnourished animals the infection appeared in 16 to 37 days, never spreading to the uninoculated eye, and persisting in the infected eye only from 17 to 90 days. There was no corneal involvement nor any macroscopic conjunctival scarring in any of the animals.

We are indebted to Dr. Howard A. McCordock for autopsy of the animals.

We are indebted to Dr. L. A. Julianelle for his cooperation and encouragement during the progress of this study.

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## NONPIGMENTED NEVUS OF THE LACRIMAL CARUNCLE

EDWARD A. SHUMWAY, M.D.

PHILADELPHIA

A case of nonpigmented nevus (lymphangioma) of the caruncle is reported, in a woman 46 years of age. The growth had been noticed for 12 months; it was excised under local anesthesia; there has been no recurrence. The origin of the nevus cells is discussed briefly and authorities quoted. Mention is made of recent theories of Masson and of Laidlaw and Murray, connecting pigmented moles (nevi) in mammals with tactile spots in reptiles and amphibia. Read before the Section on Ophthalmology, College of Physicians, Philadelphia, March 15, 1934.

Tumors of the lacrimal caruncle are comparatively rare, and are usually classified with those of the neighboring plica semilunaris. As the caruncle is a modified skin structure, containing sebaceous glands, hair follicles, hairs, and modified sweat glands, on a cushion of fat and connective tissue, and is covered by a thick layer of stratified epithelial cells, which are much more like those of the skin than are the cells of the conjunctiva, it may be involved by most of the tumors which appear in the skin itself. These growths may be either benign or malignant. To the first belong congenital nevi, dermoids, and lipodermoids, dermoid cysts, fibromas, angiomas, lymphomas, lymphangiomas (cysts), papillomas, and adenomas. The malignant types are represented by epitheliomas, arising from the surface epithelium, carcinomas from the various glandular structures, and sarcomas.

It is of interest to note that a number of cases have been reported by members of this Section. A case of primary carcinoma of the caruncle was reported by de Schweinitz<sup>1</sup> before the American Ophthalmological Society in 1898; Clarence Veasey<sup>2</sup>, who is now in Spokane, reported one of the few cases of sarcoma of the caruncle in the same year, and in 1902, a case of adenoma<sup>3</sup> developing from the sweat glands, sections of which I made and have in my collection. In 1901, Posey and I<sup>4</sup> showed before the Section a typical papilloma. Last year Derrick Vail, Jr.<sup>5</sup>, of Cincinnati, read a paper on mixed (teratoid) tumors of the caruncle before the Section on Ophthalmology of the American Medical Association, giving a bibliography in addition to the cases listed in Saemisch's elaborate article in the

Graefe-Saemisch Handbuch, and in Parson's Pathology of the Eye. The subject has been reviewed also by Victor Morax in his "Cancer de l'appareil

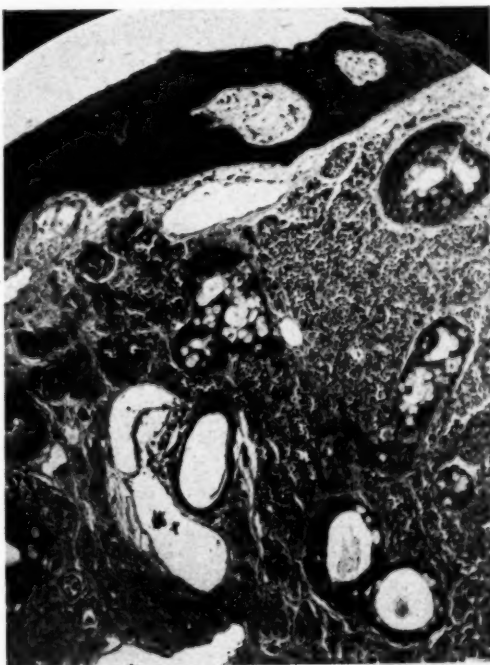


Fig. 1 (Shumway). Photomicrograph of a section from the nonpigmented nevus of a lacrimal caruncle.

visuel," published in Paris in 1926, and also by G. M. Serra in Italian (Boll. d'Ocul., 1928, v. 7, p. 783).

The growth which I am reporting was removed at the Lankenau Hospital on February 19, of the current year, from the right eye of a woman, 46 years of age. It had been noticed for 12 months, was about the size of a small pea, protruded above the level of the lid margins, causing local irritation and

discomfort, and was covered by a layer of dried secretion which, on removal, showed a granular surface. It was excised under local anesthesia, the base cauterized by the actual cautery, and the surface covered by conjunctiva which was dissected up from the eyeball and sutured into the internal canthus.

Sections of the growth were made at the Lankenau Hospital Research Institute, and studied by Drs. Reimann and Macfarland. The usual structure of the caruncle was apparent, with its sebaceous and serous glands, and hair follicles, covered over with epithelium which showed some prolongations into the underlying tissue. The tumor itself was composed of nests of cells enclosed within well-defined capsules of connective tissue, these structures being usually round in shape and varying in size from a small arteriole to a good-sized venule. The cells were small, with little protoplasm and heavily stained nuclei, in many instances appearing to be lining cells of definite spaces, but, in addition, showing a tendency to stream out into the surrounding tissues in groups and nests. No pigment was present in any part of the section, and diagnosis of nonpigmented nevus is evidently justified.

The structure was exactly similar to that seen in cases of nevus of the conjunctiva, many of which have been reported, some being pigmented, growing from small pigmented spots on the scleral conjunctiva, others entirely without pigment. So far, there has been no evidence of a recurrence.

The origin of the nevus cells has always been a matter of dispute. They are exactly like the nevi of the skin, most of which are pigmented. The cell type is rather endothelial in character, with a small amount of protoplasm surrounding a densely stained nucleus, whereas the epithelial cells, as they develop in epitheliomas, have usually a greater amount of protoplasm and smaller, less deeply stained nuclei. Usually no direct connection can be found between the nests of cells and those of the surface epithelium, even in instances when the latter, because of local irritation, sends shoots downward in the

form of processes, in which the cells may show mucoid degeneration, with formation of goblet cells, and so forth. Unna<sup>6</sup>, however, and certain dermatologists, have always defended the epithelial origin of the cells, while Ribbert<sup>7</sup> and others have expressed themselves in favor of a connective-tissue or mesoblastic origin. Von Recklinghausen<sup>8</sup> thought they arose from the endothelial cells of the lymph vessels and called them lymphangio-fibroma.

Among the ophthalmologists, Panas<sup>9</sup> and the French school considered them carcinomatous, and Leber<sup>10</sup> had the same belief. On the other hand, Wintersteiner<sup>11</sup>, Fuchs<sup>12</sup>, and Foster<sup>13</sup> could not connect the cells with the surface epithelial cells, and, with Greeff<sup>14</sup> and Axenfeld<sup>15</sup>, considered them of mesodermal origin. Pindikowski<sup>16</sup> thought they arose at times from the epithelium, at others from the consecutive tissue. The question is by no means settled as yet. My personal opinion leans toward a mesoblastic origin, as many cases later develop into melanotic growths, in which the cells appear typically sarcomatous in character.

An interesting recent development in general pathology is in a paper on "Melanomas. A Theory of Pigmented Moles. Their Relation to the Evolution of Hair Follicles," written by Laidlaw and Murray<sup>17</sup>. They showed by photomicrographs of silver-stained sections, that pigmented moles (which are nevi) are rich in nerve fibers and tactile cells. The end bulbs of nerve fibers make direct contact with nevus cells, exactly as they do with the tactile cells of the epidermis and of the hair follicles, and they confirmed observations by Masson<sup>18</sup> of a profusion of structures resembling meissnerian tactile corpuscles in certain pigmented moles.

In its elevation, pigmentation, innervation, and the groups of tactile cells in the corium, the pigmented mole bears a striking resemblance to the tactile spots of reptiles and amphibia.

In the course of evolution the reptilian tactile spots were replaced by mammalian hair follicles. These writers believe that the pigmented hairy mole is a link or transition from the pig-

mented tactile organs of the reptilian type, to hairy tactile organs of the mammalian type. In its hair follicles, it is mammalian, in its pigmentation, eleva-

tion, and in the groups of innervated tactile cells in the corium it follows the amphibian and reptile pattern.

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# NOTES, CASES, INSTRUMENTS

## CLINICAL DEMONSTRATION ON THE OCCASION OF THE VISIT OF THE INTERSTATE POST-GRADUATE MEDICAL ASSOCIATION OF NORTH AMERICA\*

PROF. DR. A. VOGT and DR. H. SCHLÄPFER  
ZÜRICH

On June 14, 1934, the Interstate Post-graduate Medical Association of North America was entertained by Professor Vogt and his assistants. The following cases and demonstrations were presented.

### 1. Tuberos sclerosi of the brain, with retinal changes

The characteristic signs and symptoms of tuberos brain sclerosis are retarded mental development, epileptic seizures and sebaceous adenomas of the face. In 1921, Van der Hoeve described certain retinal tumors as occurring only in this condition.

The case demonstrated shows, in addition to the first mentioned symptoms, a number of such tumors in the retina. The largest is in the right eye, situated slightly above and on the temporal side of the papilla. It resembles a white strawberry or a number of small white pearls. It is one and one-half disc diameters in size and projects three or four diopters into the vitreous. Some small blood vessels pass through and over the tumor. Two other very small tumors of the same white color as the first are found on the lower nasal border of the papilla, projecting one diopter. The fundus of the left eye shows three small similar but flat white spots in different regions near the macula.

The patient has no complaint to make with regard to vision and the visual acuity is normal. The general condition and also the retinal tumors have remained nearly stationary during the last eight years.

Van der Hoeve was able to examine a case histologically and found the tumor

\* Contributed by Dr. Charles A. Young, Roanoke, Virginia.

to consist of a mass of neurocytes showing no differentiation into glia cells or ganglion cells. Nerve fibers were found intermingled with these cells. Blood vessels were infrequent, pigment and other retinal elements were absent.

### 2. Detachment of the superficial lamella due to senile degeneration of the anterior lens capsule (Slitlamp demonstration)

After dilatation of the pupil a slightly opaque disc is seen on the anterior surface of the lens, in the center. This disc is the size of a normal pupil and has curled, anteriorly everted margins. It consists of a large number of small opaque blue points. Surrounding the disc, in the region where pupillary movements normally occur, a dark transparent zone is seen. Outside this again, peripherally, similar changes to those in the center of the capsule are found; a series of patches with ragged, everted edges, composed of small blue points, forming a broken ring. This ring is partly covered by the iris. There are a number of blue flecks like cotton flecks hanging onto the margin of the iris.

Clinically the condition often produces glaucoma. It can be explained as a senile degeneration of the anterior lens capsule; the superficial lamella is rubbed off in the intermediary region by the normal movements of the pupillary border. Fragments of this lamella attach themselves to that border as blue flecks. These fragments can obstruct the angle of the anterior chamber and so produce glaucoma. The central area and the peripheral part of the lens capsule do not lose the damaged opaque superficial lamella, because they are never rubbed by the pupillary border.

The condition cannot be demonstrated without dilatation of the pupil which accounts for the scarcity of descriptions. Dilatation may be carried out when the condition is suspected but circumspectly and under the closest clinical control.

The etiological significance of the

condition in connection with glaucoma was first pointed out by Vogt in 1925.

**2b. Detachment of the superficial lamella of the anterior lens capsule in glassblower's cataract (Slitlamp demonstration)**

On the anterior surface of the lens a very fine transparent pellicle lies on the pupillary part of the lens capsule; its peripheral part floats in the anterior chamber and the borders are rolled in towards the axial part. It is a structureless membrane that has become detached from the lens behind the iris and has fallen forwards, so that it forms a cup with inverted margins, hanging on the middle of the anterior surface of the lens.

A macroscopic and microscopic comparison of the above two conditions shows a fundamental difference in the nature of the capsule changes. In senile detachment the superficial lamella is not only pathologically changed and partly detached, but also broken up into a number of small fragments, which is the cause of the opacity, histologically a separation into a number of very thin lamellae. On the other hand, in glassblower's cataract, a "fire-lamella," the morbid superficial capsule lamella is merely partially detached and the edges are turned into the aqueous. The lamella is compact and not broken. This is due to its different structure which is shown histologically to be much thicker and more homogeneous than in the case of senile degeneration of the capsule.

**3. The experimental production of glassblower's cataract**

The radiation of a carbon-arc lamp (40 Amp.) is filtered through a layer of 1 cm. of a solution of iodine in potassium iodide which absorbs all visible and ultraviolet rays, and further, through a layer of 1 cm. of running water to absorb the long waved infrared rays. A pure short waved infrared radiation of considerable intensity is obtained.

Irradiation of the lens of colored and albino rabbits with the above radiation results in a cataract in the posterior cortex of the lens. This cataract can be

obtained without any damage to the other parts of the eye, but only with this radiation and not with any other rays of the spectrum (except x-rays).

The cataract appears usually on the posterior pole of the lens, sometimes on the anterior pole as well, but always in the part of the lens through which the rays pass, that is, in the center of it and never peripherally where the lens is shielded from the direct rays, although exposed to the heating effect due to absorption in the iris. This is the proof that the direct action of the light on the lens is the cause of "fire-cataract" and not the heating of the iris by absorption of the rays in its pigment (as some mistakenly contend).

The experimental cataracts in albino rabbits resemble early glassblower's cataract. The only difference is that they are produced with one intensive irradiation of this particular quality and no other whereas the professional cataracts need the exposure to short-waved infrared rays during many years for their development.

Further, these short-waved infrared rays are much more intensive in the spectrum of molten glass and iron than in normal daylight, while visible and ultraviolet rays are more intensive in daylight. Therefore it must be concluded that the short-waved infrared energy is the cause of "fire-cataract" in glassblowers and iron workers.

**4. The normal yellow spot in the macula centralis retinae, seen with the red free light**

The light of a small arc-lamp passes through a colored glass containing erioviridine and copper sulphate, the two absorbing all red rays. Therefore we are able to see the fundus red-free. The blood appears black, and the whole fundus is a green-yellow. The yellow spot of the macula is seen distinctly in the living eye (direct ophthalmoscopy), and the nerve fibers of the retina can be distinguished.

**5. A new technic for operative treatment of detachment of the retina**

Instead of a diathermic needle as used by Weve, Vogt now uses a gal-

vanization-needle. He puts the anode anywhere on the surface of the sclera. The cathode in the form of a small needle pierces the sclera and the choroid to the retina, whereby the boundaries of the hole in the retina may be cauterized. The advantages are that a weak direct current one-half to one milliamperes produces about the same effects as eighty milliamperes of high frequency alternating current (diathermy). Also, the cathode produces bubbles of hydrogen in the vitreous, which are better visible with the ophthalmoscope than the marks of diathermy. The control of the puncture position immediately after the

puncture is thus facilitated.

**6. A new instrument to remove thick membranes in after-cataract and thick capsules in complicated cataract**

The instrument has the form of de Wecker's iris scissors with teeth instead of the cutting-edges. The instrument is introduced into the anterior chamber through a very small incision (1 to 1.5 mm.) and opened only when the knee sits in the limbus. The membrane can now be seized and pulled out through the very small slit, and loss of vitreous can be avoided.



# SOCIETY PROCEEDINGS

Edited by DR. H. ROMMEL HILDRETH

## MEMPHIS SOCIETY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY

April 10, 1934

Dr. E. C. Ellett presiding

### Absorption of traumatic cataract

Dr. E. C. Ellett reported on Mrs. L., who was seen first in April, 1901, aged 30 years. The right eye had been injured the day before by a particle that flew from the head of a tack hammer. The vision was 20/40. There was a small wound near the center of the cornea, a line of opacity in the lens, and what appeared to be a foreign body could be seen on the retina below the disc. Under ether anesthesia the sclera was incised, and a magnet tip introduced into the vitreous. The foreign body was removed on the third attempt. The eye healed without reaction and a month later the vision was 20/20. A year and a half later this vision was maintained, and the patient was not seen again for nearly twenty years at which time there was a slight increase in the lens opacity to the nasal side, vision 20/40. Eight years later, namely in 1929, the vision was reduced to moving objects due to the presence of a mature cataract.

About March 1, of this year iritis developed in this eye. She had about recovered now from this. In addition to the signs of iritis the capsule seemed to contain some opaque lens matter and a clear fluid. A good sized opening could be seen in the posterior capsule and there were some vitreous opacities. There was a good light reflex, but no fundus details could be made out. Vision was moving objects; tension was normal.

### Two cases of sympathetic ophthalmia

Dr. A. C. Lewis reported the case of J. W., a boy of five years who was admitted to Memphis General Hospital on January 22, 1933, with a badly

lacerated wound of the cornea of the right eye. The injury had occurred on that day while the patient was hammering on a glass bottle. Examination on January 23rd showed an incised and lacerated wound through the cornea extending from "5 to 7 o'clock" with a large iris prolapse. On the nasal side the wound extended through the conjunctiva and into the sclera but careful examination failed to show any injury to the ciliary body. It was thought best to remove the eye, but after examination and excision of the prolapsed iris it was decided to attempt preservation of a useful eye. A large conjunctival flap was brought up from below, covering the whole cornea and sutured above the limbus. One week later when the flap retracted the cornea was cloudy but appeared healthy. The inflammation subsided slowly but steadily and two weeks after the operation the boy was discharged from the hospital with the eye quiet, the upper half of the cornea clear and a dense white scar over most of the lower half. He was told to return for observation at frequent intervals and for an optical iridectomy later.

On February 22nd the eye was congested and painful, and the tension was low. Atropin, dionin, and hot packs were ordered. On March 3rd the inflammation and pain had increased. The boy was readmitted to the hospital, the eye enucleated and a glass ball implanted. Four days after the enucleation the left eye was slightly congested and sympathetic trouble was first suspected.

A day later the pupil was contracted and slight ciliary congestion present. The glass ball was removed at once and 5 c.c. of venous blood was injected deep into the gluteal muscles. The boy was kept in a dark room, frequent instillations of atropin and dionin were made and hot packs applied to the eye with great frequency. Large doses of sodium salicylate were given and daily injections of 10 to 20 c.c. of whole milk

given. Nothing seemed to have the slightest beneficial effect; an inflammatory exudate gradually closed the pupil and filled the vitreous chamber. The patient left the hospital with light perception only. A few months later this eye also was removed in another hospital by another surgeon as it was both useless and painful.

Dr. Lewis said that his second patient, Mr. E. F. W., aged 35 years, a farmer, was seen on December 6, 1933, because of dimness of vision in the left eye for six months. He remembered having been struck lightly on this eye by a piece of heavy wire shortly before vision began to fail, but as it caused no visible wound and little pain, he consulted no doctor. Examination of the eye showed no inflammation, but a cloudiness of the lens and a reduction of vision to 20/200. A diagnosis of traumatic cataract was made and he was told he would probably require a cataract extraction at a later date. The tension was then normal. He was given 5 percent dionin to use once a day in the eye and potassium iodide for internal use and told to report from time to time for observation.

On December 20, 1933, there was no improvement, or visible change in the eye and no change in treatment was made. On January 15, 1934, the eye had been painful for a week; the pupil was somewhat dilated and the tension was 55 mm. (McLean). Pilocarpine every two hours was ordered. Three days later there was no pain, the pupil was less dilated and tension was 48 mm. Eserine was substituted for pilocarpine.

On January 22nd, the tension was 50 mm. A corneo-scleral trephining was performed the next day. One week later the eye was comfortable; the tension was 18 mm. so miotics were discontinued.

On February 19th, the vision in the right eye had been failing for several days; vision, which had been 20/20 was reduced to 20/80. No pain or inflammation had developed, tension was normal. In the left eye the tension was "minus 2," there were posterior synechia and the media were cloudy. Enucleation of

the left eye was done. Salicylates and pilocarpine sweats were given for four days and the patient was then sent home.

On February 28th, the vision had improved to 20/60 and on March 7th, to 20/30 and the eye appeared normal in all respects.

**Discussion.** Dr. R. O. Rychener had charge of the first patient after April 1, 1933, at which time the left eye showed multiple ciliary staphylomata with vision reduced to light perception. Autoserum and whole blood were administered intramuscularly without effect and the staphylomata gradually ulcerated exposing the ciliary body in five places. The eye was enucleated and Dr. F. H. Verhoeff's report through the Army Medical Museum was as follows: "Massive tuberculosis of iris and ciliary body, with perforation of cornea at limbus on each side. The lens capsule has been ruptured and the lens substance largely expelled. There is extensive separation of the retina. There are subretinal tubercles, the origin of which whether from vitreous or choroid, is not obvious. One such is at the margin of the disc."

Search was made at the Pathological Institute of the General Hospital for the enucleated right eye, but the specimen had been destroyed before a microscopic report was made.

#### Retinitis pigmentosa and cataract extraction

Dr. R. O. Rychener reported on Mr. W. M., aged 56 years, who noticed when a child that he could not see well at night. About 1900, the vision got worse and he had not been able to read a paper for thirty years. A sister and two brothers were said to have the same sort of trouble.

The right eye had a nuclear cataract which permitted a view of the periphery of the fundus. There were many pigment deposits characteristic of retinitis pigmentosa. The opacity in the left eye was so great that little view of the fundus could be obtained. The tension was normal. He was advised to have the cataracts removed, though there was very small prospect of his gaining use-

ful vision. Both cataracts were removed intracapsularly in January. The fundus could then be plainly seen and in each eye the nerve was atrophic and the pigment changes reached up to the disc. At the final testing on March 10th he had vision of 6/12 partly in each eye and was able to read Jaeger 2 with glasses.

R. O. Rychener,  
Secretary.

### COLORADO OPHTHALMOLOGICAL SOCIETY

March 17, 1934

Dr. G. O. Cary presiding

#### Typical albinism

Dr. W. M. Bane presented a case of typical albinism in a patient aged 57 years. The vision was O.D. 5/60, and O.S. 1/120. There was rotary and lateral nystagmus. No history of intermarriage was elicited. There was no benefit derived from the use of dark glasses. The patient was a graduate of the Ohio School for the Blind.

**Discussion.** Dr. E. R. Neeper cited a case of albinism in a baby seen by him a number of years ago. Dark glasses were at once prescribed and worn. No nystagmus ever developed. The child had better vision than any case of albinism Dr. Neeper had ever seen. He was of the opinion that the most benefit was to be had by avoidance of light from the cradle up.

Dr. Edward Jackson said that the most rational procedure would seem to be staining of the conjunctiva with gold chloride or platinum chloride which gave no external disfigurement. Not only the iris, but the whole fundus of albinos was without pigment and needed protection from light.

Dr. W. C. Bane asked if argyrosis produced for the purpose of protection from light would not be valuable in these cases.

Dr. E. R. Neeper said that subconjunctival injections of silver nitrate would produce the necessary staining of the tissues.

Dr. W. M. Bane said that Dr. Shwab of Omaha had suggested the use of pigmented contact glasses, but that to date this had not been tried.

Dr. M. E. Marcove said that one was tempted to put on the darkest possible glass for protection, but as the vision in these cases was never good he used a lighter shade of glass to avoid reduction of vision.

#### Congenital absence of puncta

Dr. J. C. Long presented the case of a girl, aged 6 years, who had had epiphora in both eyes since birth, and the case of her brother, aged 7 years, who had epiphora of the right eye only. In the girl the lacrimal papillae were somewhat flattened and there was no evidence of punctal opening above or below in either eye. In the boy there was an opening in the left inferior papilla only, the other three being absent. The father of these children had congenital absence of all punctal openings. The father's brother (deceased) had bilateral epiphora from birth, as had also his nephew. The mother and two other children were normal. Dr. Long cited the work of Goar who treated similar cases by dissecting an artificial passage and keeping the passage open with a probe. The father had not developed ectropion because he rubbed inward toward the nose in wiping away the tears.

**Discussion.** Dr. M. E. Marcove asked if the canaliculi were also absent. Injection of lipiodol and x-ray would help to determine this point.

Dr. E. R. Neeper advised making an incision and attempting to find the channel. He cited a case of a horse on which he had operated thirty years ago for absence of puncta. He made an incision and put a cord through the channel into the nose; the cord was left in place two weeks. The canaliculus was easily found after an external opening was made.

#### Bilateral coloboma of the iris and choroid

Dr. J. C. Long also presented the case of a man, aged 50 years, in whom there was bilateral defect of the inferior part of the iris bridged across by delicate



strands of iris tissue and a large choroidal defect crossed by retinal vessels. In the left eye an isthmus of normal choroid separated two colobomatous areas. There were small opacities on the anterior surface of the fetal nuclei of both lenses. The form fields showed a defect in the superior visual field of both eyes. Corrected vision in the right eye was 1.2-3, and in the left eye 0.8-2.

He said that according to Dr. Ida Mann's new theory a coloboma resulted not from a failure of fusion of the fetal cleft, but from an abnormal resistance of the vascular network around the lens. Minute opacities on the lens capsule showed the points of contact of these resistant vessels.

#### **Congenital anomaly of the optic papillae**

Dr. M. E. Marcove presented the case of a man, aged 69 years, in whom both optic nerve heads appeared abnormally large, and had an appearance of cupping. The patient had every sign of glaucoma; shallow anterior chambers, hyperopia, cupping of both nerve heads, and the blind spots so enlarged that they resembled Seidel's sign. However, the tension had never been found to be above 15 mm. (Schiötz). The peripheral fields were normal. The vision with hyperopic correction of +4.00 D. was 1.2 in each eye. The case was presented as an interesting congenital anomaly from which glaucoma must be differentiated.

#### **Congenital paralysis of the external rectus corrected by the O'Connor transplantation operation**

Dr. M. E. Marcove said that this patient, a girl, was first seen about two years ago with the complaint that whenever she looked to the right she saw double, became nauseated, and vomited. The condition had been present for several years, but had recently become more prominent. The past history was essentially negative; there was no birth injury. On examination there was found a complete paralysis of the right external rectus with a convergent squint of about twenty-five degrees. Enophthalmos was present.

The temporal half of the iris was quite atrophic, so that the pupil was irregularly dilated and eccentric. The fundus examination was negative. The vision with correction was normal. Because attempts to grasp the external rectus with forceps were unsuccessful, on account of the iris atrophy, and because of the presence of the condition since birth, a diagnosis of congenital absence of the external rectus was considered. However, the symptoms increased in severity, the child lost weight and became extremely nervous. An operation was therefore suggested and performed eight months ago. Under local anesthesia a nonfunctioning external rectus was found. The medial halves of the superior and inferior recti were freed, passed underneath the lateral half, and attached underneath the insertion of the external rectus. A recession of the internal rectus was also done. The final result was complete relief of the convergent squint, and an ability to turn the right eye outward about twenty-five degrees. According to various authors, a rotation of fifteen to twenty degrees was considered a good result. There was no limitation of elevation or depression of the globe.

#### **Diffuse chorioretinitis or an atypical retinitis pigmentosa**

Dr. S. Goldhammer presented the case of T. P., aged 15 years, who for the past five years had noticed diminution of vision for both near and far work, and particularly, difficulty in night vision. There were also frontal headaches and mild attacks of vertigo. The family history and past history was irrelevant. The vision with moderate compound myopic astigmatic correction was, right eye 0.5+, and left eye 0.4+. There was lateral nystagmus of both eyes, not particularly increased on looking in various directions of the gaze. The fundus examination showed numerous widely scattered pigmented areas from the equator to the posterior pole encroaching on the macular area, particularly in the left eye. These pigment deposits were of the bone corpuscle type. There were also whitish, almost perfectly round spots about two

millimeters in diameter, especially numerous along both sides of the retinal vessels. There were also atrophic choroidal areas in the same situation. The discs were a little pale, and the arteries were much reduced in size. There was concentric contraction of the form fields and corresponding narrowing of the color fields. Fixation was poor because of the nystagmus. There seemed also to be scattered scotomata. The general physical examination, including the blood Wassermann, was negative. Dr. Goldhammer asked for suggestions for treatment.

**Discussion.** Drs. R. W. Danielson and W. M. Bane thought that this case resembled chorioretinitis rather than retinitis pigmentosa.

#### **Luetic iridocyclitis and neuroretinitis resistant to treatment**

Dr. J. L. Swigert presented the case of Glenn R., aged 19 years, who gave a history of Neisserian urethritis eight months prior to the onset of iridocyclitis in January, 1934. The urethritis was poorly treated and infection spread into the genital tract. An iridocyclitis failed to improve with the usual treatment of atropine, constitutional treatment, and foreign protein injections. However, the foreign protein injections were followed by a diminution in ciliary injection and absorption of the spongy gelatinous exudate in the anterior chamber, for a day or so only, to be followed by an aggravation of all signs and symptoms. Maintenance of dilatation of the pupil was particularly difficult. In February, 1934, the blood Wassermann was found to be four plus, and conservative antiluetic treatment was instituted. A slow improvement set in after initial aggravation of the iridocyclitis. At the onset the vision O.S. was 1.2 and dropped to 0.2 at the height of the iridocyclitis when the vitreous was filled with dust-like opacities, practically obscuring the view of the fundus. On March 9, 1934, the lower branch of the central retinal vein was seen to be congested, dilated and tortuous. The dilatation and tortuosity increased nasally and below the disc with edema and obscuration of the nasal

margin of the disc. The veins were deeply indented at the arterial crossings. The vision was 0.6. The next day small flame-like hemorrhages were seen nasally and below the disc along the vessels. These increased somewhat in the next few days without disturbing the visual acuity. At the present there were a few small pigment spots and a few dust-like deposits on the anterior lens capsule, and numerous small opacities in the vitreous. The retina was cloudy and edematous around the disc along the nasal and inferior vessels. The nasal portion of the disc was blurred and slightly elevated. The veins were tortuous, dilated and markedly indented at the arterial crossings, particularly in the lower fundus. There were a few small flame-shaped hemorrhages around the disc along the veins. There was accentuation of light reflexes in the macular region.

**Discussion.** Dr. W. A. Sedwick said that the neuroretinitis did not appear so limited to him.

Dr. M. E. Marcove was of the opinion that there was probably a thrombosis of the lower nasal retinal vein.

#### **Scleritis, tenonitis**

Dr. R. W. Danielson presented the case of Alma K., aged 32 years, who gave the history of onset of arthritis in June, 1933. In the latter part of September some teeth were removed, the extraction being followed by improvement of the arthritis. A month later both eyes became very red, without any pain, headache, discomfort, or discharge. The patient had arrested pulmonary tuberculosis. When first seen by Dr. Danielson in December, 1933, there was marked bluish episcleral injection without pericorneal hyperemia. The episclera appeared thickened, especially inferiorly. No other abnormalities of the eyes were noted either externally or in the fundi. The vision with slight correction was 20/20. Laboratory examination, blood Wassermann and blood count were normal. The patient was now considerably improved, but inasmuch as she was not getting well as rapidly as she desired,

Dr. Danielson planned to institute diagnostic and, if necessary, therapeutic tuberculin regime.

#### Clinical comparisons of various local anesthetics

Dr. R. W. Danielson presented a table in which he compared the local ophthalmic anesthetics as to trade names, common names, incompatibility with fluorescein and mercurochrome, compatability with mercury oxycyanide and other solutions, smarting on instillation, and subsequent drawing or astringent sensation, antiseptic value, action on the pupil, fatalities reported, and the cost.

Anesthetic	Other name	Precipitation of Mercurochrome and Fluorescein	Drawing sensation after instillation	Fatalities reported	Antiseptic action	Effect on pupil	Strength of solution used	Price per ounce
Butyn		Yes	Marked	Yes		Dilates	2%	\$1.25
Cocaine		Yes	Moderate	Yes		Dilates	4%	\$0.50
Holocaine	Phenocaine	Yes	Moderate	No	Yes		1%	\$0.35
Nupercaine		Slight	Moderate	No			1%	\$0.40
Pantocaine	Tetracaine	Yes	Moderate	No			$\frac{1}{2}$ %	\$1.50

**Discussion.** Dr. J. C. Long said that the different hydrogen-ion concentration explained the precipitation of mercurochrome and fluorescein by the local anesthetics. The anesthetics were acid in reaction while mercurochrome and fluorescein were alkaline.

Dr. E. R. Neepers said that according to Wilmer, pantocaine was more toxic than holocaine. Dr. Neepers never put anything into any eye without first washing out what might have previously been instilled.

Dr. S. Goldhammer said that according to Gifford the marked undesirable burning sensation produced by butyn was due to its acidity.

Dr. R. W. Danielson said that Dr. Elschmig combined mercury oxycyanide with butyn, atropine, and cocaine in his prescriptions.

George H. Stine,  
Recorder.

#### NEW ENGLAND OPHTHALMOLOGICAL SOCIETY

January 16, 1934

Dr. Hugo B. C. Riemer presiding

#### Lattice keratitis

Dr. Juanita P. Johns presented a 50-year-old man, who in May, 1933, had 1/200 vision in the right eye and 20/30 vision in the left eye. A diagnosis of lattice keratitis in both eyes was made. The right eye was operated upon by Dr. Verhoeff who removed anterior layers of the cornea, hoping to stop the process. After the eye had subsided the vision was 20/200. This observation

was made in June, 1933. In December, 1933, the vision was 4/200. The slitlamp examination revealed a typical picture of lattice keratitis: through the superficial part of the corneae were interlacing lines with scattered grayish nodules. The entire surface of the right cornea was involved with the exception of a narrow band adjacent to the limbus. The left cornea was clear except for an area on the nasal part opposite "6 to 9 o'clock" extending from about one millimeter from the limbus to the margin of the pupil. The pupillary area was entirely clear. In both eyes, running at different depths of the corneae, were numerous small flocculent specks of light yellowish material.

#### Lipemia retinalis

Dr. J. Herbert Waite presented a 16-year-old boy with diabetes of three years' duration. The condition was con-



trolled by diet and sixteen units of insulin daily. Although the patient admitted frequent dietary indiscretions, he never had coma. There was never any blur in vision or transitory refractive changes. On January 15, 1934, while being examined in the office of Dr. Joslin, it was noted that blood drawn for sugar determination presented a marked lipemic appearance. The fundi were then examined and found to present the characteristic lipemia retinalis. The carbon dioxide combining power was found to be 22 volumes percent. Blood cholesterin was 1600 mg. per 100 cc. Examination of the eyes revealed no abnormalities other than the characteristic appearance of the retinal vessels. The arteries and veins were not to be differentiated from each other, and looked like flat milky ribbons. The acuity in each eye was 20/20, the visual fields were full, and the blind spots were of normal size. With falling blood fats, the main retinal vessels resumed normal appearance in two days and the finer twigs remained lipemic for three days. During the week in question, another case of lipemia retinalis was found at the Deaconess Hospital on the service of Dr. Joslin, the patient being a 12-year-old boy having had diabetes for 5 years.

#### **Dislocation of lens in anterior chamber with asteroid hyalitis**

Dr. Benjamin Sachs presented a woman 38 years of age who first came to the infirmary two years ago showing dislocated lens in the anterior chamber. There was increased tension and the vision was nil. The lens was removed in capsule without loss of vitreous. Following this a large detachment of the retina was noticed. After much questioning the patient admitted being struck in the eye by a ball fifteen years previously, and that the vision was lost at that time. She had no pain in the eye. The patient was given pilocarpine but the tension was 40 mm. (Schiötz). In the past few months the vitreous and aqueous became filled with many large and small cholesterin crystals.

#### **Operations for spastic entropion and occluded punctum**

Dr. William D. Rowland said that the resection of the external canthal ligament was suggested for the control of senile spastic entropion. Based upon several observations it was determined that there was a relaxation of this ligament consistent with senile relaxation of tissues. When the external canthus was brought out to a normal position on the orbital margin the entropion was corrected. Surgical resection anchored the external canthus to its original position. This procedure might also be considered for spastic entropion. Dr. Rowland said the DeWecker scissors was suggested as being ideally suited for right-angled incisions of the punctum when there was either occlusion or eversion resulting in epiphora. The blades were small and the angle of the scissors lent itself very much better to mechanical manipulation than ordinary scissors in making the very exact incisions necessary for the success of the procedure.

James J. Regan.  
Recorder.

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### **ST. LOUIS OPHTHALMIC SOCIETY**

March 23, 1934

Dr. E. C. Spitze, president

#### **Postoperative results of Elschmig's clinic**

Dr. L. C. Drews presented two cataract cases operated on by Dr. Elschmig. He stated that before operation all patients had had a complete dental examination, x-ray of sinuses and nasal examination in addition to a general examination. After the operation all patients were kept in bed four days although Dr. Elschmig had stated that they could be up on the first day. On the second day the dressings were changed and homatropin was used sparingly. The unoperated eye was uncovered on the fourth day but Dr. Elschmig usually left this eye open on the second or third day. On the sixth or sev-

enth day the patients were allowed to get up and the sutures were removed. On the tenth day, the patients were discharged from the hospital and atropin was used in the operated eye.

There had seemed to be some doubt about the advisability of using tincture of iodine along the conjunctival wound, but in the cases which he had seen, there was only a very slight reaction which could have been attributed to the use of iodine. Only a small amount of secretion was present when the eyes were first dressed.

**Discussion.** Dr. F. E. Woodruff commented upon the fact that the vision obtained after the operation was not as favorable as might be expected from the appearance of the eyes, and asked if slitlamp examinations had been made.

Dr. J. H. Gross stated that it was very disappointing that the visual results were not better. In as much as it had been claimed that in intracapsular operations a better pupil and better vision were obtained, he would have ex-

pected better vision than 20/30, and he would consider that the extracapsular operation was preferable.

Dr. Lawrence Post said that the superior rectus stay suture, as used by Dr. Elschmig, gave a feeling of security in holding the eye, but in using it, a trained assistant was needed. He also commented upon the fact that there seemed to be definite pain when the retrobulbar injection was made. He stated that he injected the fluid very slowly and in this way caused very little pain. There was also much less danger of hemorrhage with slow introduction of the needle.

Dr. John Green stated that there seemed to be a difference of opinion as to how much time should elapse between the retrobulbar injection and the operation. In performing enucleations he had waited as long as thirty minutes, which might have been unnecessary, but he believed that five minutes was too short a period.

J. F. Hardesty,  
Editor.

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## DEMONSTRATION OF INSTRUMENTS

One of the very important features of every medical meeting is the display of ophthalmic instruments and appliances. A particularly interesting assortment was on view at the meeting of the Academy in Chicago in September. Many ophthalmologists await medical meetings before buying equipment because of the unusual opportunity then to view the offerings of the different manufacturers. As in all matters of selling, psychology is a vital factor. Many elements enter into this; not the least important being the situation of the room in which the booths are placed. The location in Chicago was ideal. The room adjoined the convention hall so it was necessary to pass through it to reach this hall from the elevators. This prevented any possible failure to see the exhibits. An additional feature of great value was the existence of a central enclosure in which were about twenty or thirty comfortable chairs. This rendered

the room conducive to relaxation and the casual interchange of ideas, so important at medical meetings. It was most convenient, when happening on a friend, to be able to gravitate to the rest enclosure and talk for a while. Then it was natural, after a short rest, to repair again to the instrument booths for further talk with the demonstrators and study of their displays.

Among the interesting appliances shown were the new miniature cameras for external photography. The Contax and Leica were examined by many. A practical illustration of the advantages of a simple and inexpensive projection apparatus with which a film instead of plates may be used, at about one-fifth the cost of the latter, was given by the author of one of the papers. Fundus cameras are coming more and more into use and the instruments showed definite improvements. Representatives were constantly being requested to demonstrate the new eikonic apparatus and the stereo-orthopter. Clinics for



study of the imbalances of the extra-ocular muscles are becoming numerous, so instruments for fusion training received more than usual attention. Sets of charts and special stereoscopes have been increasing rapidly in popularity. A lamp for localizing the lens when dislocated into the vitreous and a new hand slitlamp, as well as many beautiful new operating instruments, were on view. An eye pad which is to be heated in boiling water and is said to retain heat for an hour, appears to offer an excellent method of applying prolonged wet heat.

Beautiful artificial eyes and glass models of eye diseases were on exhibit and the demonstrators spoke of the feasibility of constructing glass models for classroom work. More than one hundred such eyes are represented in a collection in the Surgeon-General's Library.

The latest wrinkles in efficient lenses were presented and the merits of tinted lenses depicted.

Though tremendously impressed by the marvels of modern optical instruments, to the interested observer there was another feature of the manufacturer's exhibit that was equally striking; namely the terrible inefficiency of the presentation and the waste of human energy. No one could guess the number of times that the very same demonstration was repeated. No sooner was the company representative finished with the description of a certain instrument to one physician than another one or two would gather around and the whole story had to be told again. This went on for the entire five days of the meeting and in the end only half of the story had been told to about half of those who would have liked to have heard it.

To obviate some of this waste the editor suggests that each exhibitor be allowed stated periods in which he can present his instruments in a convention hall before the entire assembly of those interested. The time of the demonstration would be announced in the program and the special instrument to be shown would be listed. In this way a satisfactory description of the appara-

tus would be given to everyone interested and a most admirable feature, both from the point of view of the society member and of the instrument maker, added to the program. At times when the ophthalmological papers were being read the nose and throat instruments could be shown and when the nose and throat program was being given the eye instruments could be demonstrated or if preferred, since most of the Academy members practice both ophthalmology and oto-laryngology, other periods could be utilized; possibly during some of the evenings. Most of the society would prefer this type of evening to social entertainments which are difficult to plan and are attended, chiefly because of loyalty to the Society, by scarcely one half of the group.

Lawrence T. Post.

#### FOCAL INFECTION OR UVEAL TUBERCULOSIS

Strictly speaking, tuberculosis as it appears in the eye is commonly to be included among the "focal infections." But in using the latter expression we more often have in mind nontuberculous infections which have been transferred through the circulation from other parts of the body.

A quarter of a century ago it was still quite general to class as "rheumatic" those inflammatory conditions of the anterior uveal tract whose cause was not clearly understood. The work of Rosenow and others revolutionized our conceptions as to these disorders. Particularly incriminated were infections around the roots of the teeth, although many cases of "focal infection" were attributed to the tonsils, the accessory nasal sinuses, and the genital organs, as well as various other parts of the body.

In etiology and therapy new enthusiasms are frequently overdone, and even in the English-speaking countries we are becoming perhaps a little more conservative as to our interpretation and treatment of chronic or semichronic uveitis.

Germany and some other European countries have never been very sympa-

thetic toward what has been called, sometimes with a touch of scorn, the American point of view. German writers on the subject, especially, have been disposed to classify as tuberculous many cases of the type which in the United States have led to removal of teeth or tonsils.

A recent paper by Karl Schmidt (*Klinische Monatsblätter für Augenheilkunde*, 1934, volume 93, page 19), although still rather frankly skeptical, displays a somewhat more tolerant and receptive attitude. Schmidt does at least propose thorough investigation and recording of the evidence as regards the responsibility of the teeth for ocular infections. He would only accept as cured those eye cases which have been under observation for fully a year after treatment of the teeth. He thinks that it remains to be ascertained whether treatment of the dental roots will prove as serviceable as extraction. He urges the importance of roentgenologic investigation as to the presence of old lung tuberculosis, although he admits that it is theoretically quite conceivable that a patient with an old and practically inactive lung tuberculosis may develop an iritis which is due to a granuloma of a dental root.

It is interesting to note that Argañaraz of Buenos Aires, in one of the best recent textbooks on ophthalmology (see *American Journal of Ophthalmology*, 1932, volume 15, page 1080), adopts the North American viewpoint and frankly inculcates teeth, tonsils, nasal sinuses, and the genitals.

If American clinicians and writers have been a little too enthusiastic as to the part played by miscellaneous focal infections, a few German workers have certainly gone to the other extreme in blaming the vast majority of obscure anterior uveal disturbances on tuberculosis. An example is Koeppe, whose early studies with the biomicroscope procured him some fame, and whose name has been attached to a type of minute nodule found near the sphincter margin of the iris. Koeppe went so far as to regard such nodules as invariably pointing to tuberculosis as the basis of the uveal involvement. But this opinion

has been rather widely discredited or at least viewed with skepticism. German interpretation of obscure cases of anterior uveitis as tuberculous seems largely to be based upon a negative Wassermann reaction and a positive tuberculin reaction, and less uniformly upon roentgenologic evidence of old lung tuberculosis, rather than upon investigation as to the possible responsibility of other forms of focal infection.

Early last year the *American Journal of Ophthalmology* (1933, volume 16, page 350) called attention to Schieck's description of a method of treatment of tuberculosis of the anterior segment by first evacuating the aqueous humor from the anterior chamber with a syringe and then at once replacing the aqueous with blood obtained from one of the patient's veins. Since Schieck's first paper was read before the German Ophthalmological Society, the topic has been discussed by several writers, chiefly Schieck's associates or pupils. One of the latter, Garcia Miranda (*Archivos de Oftalmologia Hispano-Americanos*, 1934, volume 34, page 349) has recorded the late results observed in twenty cases treated by this method in Schieck's Würzburg clinic. All the cases were diagnosed as tuberculous, although the published evidence on this score is by no means uniformly positive.

In thirteen of the cases described, a single injection of blood into the anterior chamber was sufficient to produce disappearance of the inflammatory phenomena. In other cases relapses were overcome by repetition of the treatment. Disturbing complications were not encountered.

Garcia Miranda suggests that it would be interesting to study the effect which injection of the patient's blood into the anterior chamber would produce in nontuberculous iridocyclitis. While feeling some doubt as to the uniformity with which the basic etiology in Schieck's cases was correctly interpreted, American clinicians may consider the advisability of employing Schieck's autohemotherapy as an additional method in the treatment of obstinate cases of anterior uveitis.

W. H. Crisp.

### MEETINGS AT BUTTE

The Annual Meetings of the Pacific Coast Oto-Ophthalmological Society, and the Western Ophthalmological Society, were held this year at Butte, Montana, July 16-19 inclusive. Examinations were held by the American Boards, on the 16th for Oto-Laryngology, and on the 17th for Ophthalmology. At the latter sixteen candidates took the examination.

Papers devoted to Ophthalmology included: In the Pacific Coast Society, Diseases of the pituitary region by Walter Cameron, of Tacoma; The Curran operation for glaucoma, by Roderic P. O'Connor, of San Francisco; How I do a refraction, by Donald H. O'Rourke, of Denver; Aspects of the treatment of corneal ulcers, by A. R. Irvine, of Los Angeles; The treatment of strabismus, with recent work on orthoptic training, by Sanford R. Gifford, of Chicago; Choice of an intracapsular extraction method by the average oculist, by Marc Anthony, of Spokane; Ocular glandular tularemia complicated by nasal diphtheria, by Horace G. Merrill, of Provo, Utah; A lecture on light and lighting of Cleveland, Ohio, by M. Luckiesh, of the Nela Research Laboratory, Cleveland, Ohio.

In the Western Ophthalmological Society, the address of the President, Dr. John E. Weeks, of Portland, Oregon, dealt with, The development of ophthalmology and other branches of medicine, especially in America. The papers included: Problems of heterophoria, by Luther C. Peter, of Philadelphia; Recession operation for squint, by Joseph L. McCool, of San Francisco; Orthoptic training for squint, by George N. Hosford and Avery M. Hicks, of San Francisco; A case of retino-blastoma, by A. Ray Irvine of Los Angeles; Spontaneous absorption of intraocular copper fragments, by Frederick C. Cordes, of San Francisco; Adolescent glaucoma, by Harry V. Würdemann, of Seattle.

John M. Wheeler, of New York took up, Interesting problems calling for plastic surgery of the eyelids, and he explained with lantern slides his methods of dealing with them. Transplanta-

tion of ocular tendons was discussed by Roderic O'Connor, of San Francisco. Amateur photography of the exterior of the eye, was explained and illustrated by William C. Bane, of Denver; both for white and black, and for colored photographs. A case of Double traumatic cataract, was reported by John A. Donovan of Butte. Many foreign bodies were removed from the iris and cornea, and removal of the cataracts gave good binocular vision that had enabled the man to continue his work as a book-keeper for many years.

Tumor of the optic nerve (Glioma), was reported by Frederick A. Kiehle, of Portland. Aberrations of ocular refraction, was the subject of a paper by Edward Jackson, Denver. This paper and others, especially those on operations for squint, were discussed by Dr. Walter B. Lancaster, of Boston. Some of these papers will be published in this Journal. All of them with the discussions they elicited will appear in the Transactions of the Society.

A notable feature of these meetings was the examinations, held by the American Boards of Ophthalmology and Oto-Laryngology, each represented by five of its members. These examinations were held in the Murray Clinic, organized and established before the Mayo Clinic of Rochester, Minnesota. The meeting was the twenty-first annual meeting of the Pacific Coast Oto-Ophthalmological Society, which now includes more than three hundred members.

It was the first scientific meeting of the Western Ophthalmological Society, but made memorable by the presence and active participation of men who have been active in the national organizations. These included the President of the American Ophthalmological Society, and two of its former presidents; the President of the American Academy of Ophthalmology and Oto-Laryngology, and five of its former presidents. There were three former chairmen of the Section on Ophthalmology of the American Medical Association in attendance and taking part in the program. The development and specialization in modern medicine, re-



ferred to in Dr. Weeks' address, was well illustrated by the gathering at Butte of so many ophthalmologists. When the American Ophthalmological Society first met in New York in 1865 there were but five who attended the meeting, and the first president of the Society never confined his practice to ophthalmology. At that time all the surgeons to Wills Hospital were general surgeons. The Western Ophthalmological Society starts with a membership of over fifty, including two members in Honolulu.

The next annual meeting will be held in Portland, Oregon. The exact time will be announced, when arranged in conjunction with the Pacific Coast Oto-Ophthalmological Society, which will meet at the same place.

Edward Jackson.

### BOOK NOTICES

**Atlas Fundus Oculi.** By William H. Wilmer, M.D. One hundred colored plates. 139 pages of text. Price \$35.00. The Macmillan Company, New York, 1934.

This is one of the most beautiful atlases of the fundus of the eye that has ever been published. The introductory chapters describe the manner of presentation, including general remarks on the fundus and methods of examination.

The hundred exquisite illustrations have been painted from actual cases by Mrs. Annette S. Burgess. On the page facing the illustration, which is protected by a suitable tissue paper insert, is a very condensed but quite adequate clinical history, general physical examination with the results of all special tests, and a careful description of the fundus picture. In many cases the clinical outcome is given. This adds materially to the interest. In a few instances the same eye is depicted at different stages in the progress of the disease.

The author has shown a real gift in the choice of expressions descriptive of the intraocular findings and excellent phrases are substituted for time-worn descriptions.

All of the usual fundus conditions are depicted. In addition a few rare ones are included. The insertion of paintings of the fundi of common laboratory animals is a valuable feature.

There is little to be said in adverse criticism. The discs are possibly too uniformly colored, failing to show the structural elements as distinctly as they are seen with the ophthalmoscope. Tuberculin tests were almost always made and recorded as positive or negative to various amounts. It is stated that the intracutaneous diagnostic method of Denys was used. A statement as to the diagnostic value attributed to this test would be of interest.

The possession of this beautiful volume will be a delight to every ophthalmologist who is fortunate enough to procure one, of value to himself personally and of great importance in teaching.

Lawrence T. Post.

**Diseases of the eye.** By Charles H. May, M.D. 496 pages, 376 illustrations including 25 plates with 78 colored figures. William Wood and Co. 1934. Price \$4.00.

This perennial favorite of the medical student and general practitioner appeared in its fourteenth edition in August of this year. This edition follows the thirteenth which appeared in 1930, was reprinted in 1932, and in 1933. In this year the seventh British, the ninth Spanish, the sixth Italian, and the third Chinese editions were issued.

The fourteenth edition contains some new material with the substitution in other cases of new for old. It has been brought fully up to date and deserves the prominent place in ophthalmology which this textbook has always had.

Lawrence T. Post.

**Al-Morchid Fi'L-Kohl (The ophthalmic guide).** By Mohammad Al-Ghâfiqî. Translated into French by Max Meyerhof. 225 pages, 16 illustrations. Laboratoires du Nord de L'Espagne, Masnou - Barcelona, 1933.

This is a beautiful volume with an embossed parchment cover. It presents

in full the translation into French of the original Arabian manuscript.

It is somewhat discouraging to those who unearth rare ophthalmic literature to find invariably that the book had been previously discovered and abstracted by that diligent and astute student of ophthalmic literature, Hirschberg. He however was content to review only a part of this volume so that much of it has remained untranslated until this publication of Dr. Meyerhof.

It is always entertaining to read of the methods of earlier days. This book, written in the twelfth century, contains matter of real interest. A few illustrations are included; among them the instrument for couching the lens and various types of scalpels. Naturally external diseases receive a far more important part than in most textbooks of today. Drugs and ointments hold a prominent place, many of them obviously could have very little value. Their multiplicity as described in this and the well known older German treatises possibly gives rise to the current expression of "eye-wash." Probably the most interesting chapter is the last one which contains a detailed description of an operation for cataract. Attention to the weather is an interesting detail. The patient was advised to avoid operation when the south wind blew. This was because such a wind was hot and loaded with dust while the wind from the north was cool and clear.

The profession is indebted to the man who has taken the pains to make such a translation as this. It can be only a

labor of love as probably not many will peruse even the translation but to have it available to those who are interested in the history of ophthalmology renders the contribution a valuable one.

Lawrence T. Post.

### CORRESPONDENCE

Correction for Dr. O'Connor's paper on cataract extraction in the September 1934 issue of this Journal.

"In reading over the reprint of my cataract paper I found an editorial alteration in a sentence which destroyed its meaning. The sentence was 'ophthalmic surgery should be looked upon in the same relation that general surgery bears to medical practice,' by 'relation' I meant to general ophthalmology. The alteration compared ophthalmic surgery to general surgery and read as follows: 'ophthalmic surgery should be looked upon as having the same relation to general surgery as the latter bears to medical practice.'

"My idea is that ophthalmology should be divided into surgical and non-surgical and an individual who can't operate should recognize the fact and refer operative work to one who can.

"Could you make a correction somewhat as follows, 'Ophthalmic surgery should be looked upon as having the same relation to the practice of ophthalmology as general surgery bears to medical practice.' I should have written it that way in the first place."

Very truly,

(Signed) Roderic O'Connor.

# ABSTRACT DEPARTMENT

EDITED BY DR. WILLIAM H. CRISP

Abstracts are classified under the divisions listed below, which broadly correspond to those formerly used in the Ophthalmic Year Book. It must be remembered that any given paper may belong to several divisions of ophthalmology, although here it is only mentioned in one. Not all of the headings will necessarily be found in any one issue of the Journal.

## CLASSIFICATION

- |  |  |
|--|--|
| 1. General methods of diagnosis                        | 10. Retina and vitreous                        |
| 2. Therapeutics and operations                         | 11. Optic nerve and toxic amblyopias           |
| 3. Physiologic optics, refraction, and color vision    | 12. Visual tracts and centers                  |
| 4. Ocular movements                                    | 13. Eyeball and orbit                          |
| 5. Conjunctiva   | 14. Eyelids and lacrimal apparatus             |
| 6. Cornea and sclera                                   | 15. Tumors                                     |
| 7. Uveal tract, sympathetic disease, and aqueous humor | 16. Injuries                                   |
| 8. Glaucoma and ocular tension                         | 17. Systemic diseases and parasites            |
| 9. Crystalline lens                                    | 18. Hygiene, sociology, education, and history |
|  | 19. Anatomy and embryology                     |

### 6. CORNEA AND SCLERA

Ambler, J. V. and Van Cleve, J. V. **Malarial therapy in syphilitic interstitial keratitis.** Jour. Amer. Med. Assoc., 1934, v. 102, May 12, p. 1553.

Seventeen patients with syphilitic interstitial keratitis, whose ages varied from seven to thirty-five years, were treated by means of malarial therapy, with uniformly good results. The rapid and complete cessation of pain, photophobia, and lacrimation in every case, usually early in the course of the treatment, is emphasized as the most important finding of this study. The final result in all cases was very good. Malaria therapy was found most gratifying when used in somewhat chronic cases. Four of the cases were of over one year duration, one case having persisted for seven years. In none of the cases was there permanent impairment of vision sufficient to cause an industrial handicap. Malaria is not advocated in cases showing only residual scarring of the cornea, but in chronic cases that still present pain and photobia it invariably causes these symptoms to cease. It is believed that the corneal opacities are more rapidly and completely absorbed than after any other type of therapy. Recurrence was noted in only two cases; in each case it occurred a few weeks after the malarial therapy and

responded well to the usual antisyphilitic treatment. Five patients each had only one eye involved when malarial therapy was administered; in none of these did the second eye become involved. Ten patients had received varying amounts of antisyphilitic treatment prior to the malaria, and seven had received no treatment of any kind. There was apparently no difference in the response of the two groups. There were no fatalities, and in only one case did alarming symptoms develop which necessitated termination of the malaria early in the course. In the authors' experience children under eleven tolerate malaria poorly, but in these cases the milder forms of fever therapy, such as typhoid vaccine, are usually quite successful. The technique is given in detail.

George H. Stine.

Bietti, G. **The pathologic anatomy of corneal degeneration of the speckled type (Fehr).** Rassegna Ital. d'Ottal., 1934, v. 3, March-April, p. 241.

Bietti's patient was a laborer of forty-two years whose vision had first begun to fail at eighteen. His family and personal history were negative, as was his general physical examination. The corneal disease was of the speckled form described by Fehr in 1904 and considered to be of the familial type. The



author presents the first histological report of the corneal tissue in this condition. The changes found were quite similar to those described in cases of nodular and reticular degeneration of the cornea, differing in only one respect. In the degenerated zone were present two substances, one acidophilic and one basophilic, the latter presenting staining peculiarities of mucin. The author would thus group the nodular, reticular, and speckled types under the comprehensive name of "hyalin-mucin dystrophy of the cornea, usually familial".

Eugene M. Blake.

Caramazza, F. **Concerning Krukenberg spindles.** Arch. di Ottal., 1934, v. 41, Jan.-Feb., p. 1.

Two cases of Krukenberg spindle are described, in women aged fifty and fifty-one years respectively, both of whom had dark brown irides. The refractive error in the two eyes was equal in each case; in the first being simple myopia of one diopter, the second, simple myopic astigmatism of two diopters. The author is of opinion that some acquired cause produces disintegration of the uveal pigment and damaging of the endothelial cells, permitting the pigment to impregnate the cells.

Herman D. Scarney.

Croci, L. **Histologic research following the Knapp method of corneal tattooing with gold chloride.** Lettura Oft., 1934, v. 11, March, p. 109.

Tattooing was performed on seventeen rabbits, divided into four series, viz., normal corneae, corneae with simple leucomata, corneae with vascularized leucomata, and earneae with adherent leucomata. The color produced in normal cornea is constant, a very dark grey, remaining unaltered after five months. In leucoma it is much less constant and sometimes insufficient: frequently a clearing up process is seen, especially in vascularised leucomata.

The gold assumes a conical disposition with its base anterior. The gold chloride is precipitated generally in the form of very fine granules, but in leucomata, especially in the vascularized type, it sometimes arranges itself in

more or less large masses. In the normal cornea the gold is found more deeply situated than in the leucomatous cornea. In some cases, especially of vascularized leucoma, the superficial strata are devoid of gold, which is found only in the middle layers. (Microphotographs, bibliography.)

F. M. Crage.

Galante, E. **The action of ultraviolet rays upon corneal affections and injuries.** Rassegna Ital. d'Ottal., 1934, v. 3, March-April, p. 187.

In his studies of the therapeutic action of ultraviolet rays upon corneal tissue, Galante employed the radiation lamp of Birch-Hirschfeld, which furnishes rays of from 450 to 280 millimicra. Applications were made first for one minute and then gradually increased to five minutes. The treatments were given daily, alternate days, or every third day, 102 cases of various types of corneal lesions being treated. Twelve rabbits were subjected to corneal trephining, and histological studies made. The author concludes that proper use of ultraviolet therapy results in more prompt arrest of the inflammatory process, rapid resorption of exudate, arrest of new vessel formation, and energetic stimulation of the normal anatomic elements of repair, in particular the corneal epithelium. (Four illustrations.)

Eugene M. Blake.

Gallenga, C. **Injections of yellow oxide in the treatment of interstitial keratitis.** Rassegna Ital. d'Ottal., 1934, v. 3, March-April, p. 295.

For fifty years Gallenga has employed very successfully an aqueous solution of yellow oxide of mercury intramuscularly in congenital luetic keratitis. Injections are made weekly. No reaction or abscess ever occurred. The formula is as follows: Finely powdered, pure yellow oxide of mercury, 1.00; powdered and sterile gum arabic, 0.30; distilled water, 30.00. One to two c.c. is used for injection intramuscularly.

Eugene M. Blake.

Handmann. **Apparatus for treatment of episcleritis by means of suction.**

Klin. M. f. Augenh., 1934, v. 93, July, p. 86.

Suction is applied for one or two minutes to an area of episcleritis by means of a small glass bell which is in communication with a record syringe by means of a rubber tube. Five or six treatments in the course of two to three weeks usually suffice. The author thinks the method definitely useful.

F. H. Haessler.

Kayser, B. **Remarks on Friede's megalocornea theory, etc.** Klin. M. f. Augenh., 1934, v. 93, May, p. 655.

Kayser objects that Friede imputes to him the belief that the cornea is part of a perfect sphere in megalocornea merely because Kayser uses the commonly accepted term cornea globosa. He believes that Friede does not adequately support the theory that in megalocornea a reciprocal relation exists between the size of corneal content and the content of the posterior segment. Since megalocornea is a sex-linked recessive characteristic it can hardly be considered the primitive type.

F. H. Haessler.

Mann, I., and Baker, D. **Agranulocytic anemia following herpes ophthalmicus.** Brit. Jour. Ophth., 1934, v. 18, Aug., p. 458.

A woman 38 years of age was treated for a severe right-sided ophthalmic herpes from which the ocular complications had not cleared up after two months. She gave a history of severe nervous attacks and the use of barbiturate drugs. Subsequently she developed a sore throat, enlarged submaxillary glands, and a temperature of 101.5 F. Blood examination showed red cells four million, white cells five hundred. A diagnosis of agranulocytic angina was made. Six days later the patient developed pneumonia and died.

D. F. Harbridge.

Nižetić, Zdravko. **A modification of Filatow's keratoplasty.** Klin. M. f. Augenh., 1934, v. 93, July, p. 89.

For the small ivory plate Nižetić substitutes a knife which has dull parallel

edges and ends in a triangular point. The knife is inserted into the cornea and left until the operation is complete. It shortens the operation, prevents loss of aqueous, and serves to fix the eyeball perfectly. Neither fixation forceps nor bridle sutures are necessary.

F. H. Haessler.

Stallard, H. B. **"White rings" in the cornea.** Brit. Jour. Ophth., 1934, v. 18, Aug., p. 452.

The author's patient was a boy aged seventeen years. The eyes were quite normal except for a broken oval ring of white dots 2 by 0.15 mm., situated in the upper temporal quadrant of the right cornea, 2 mm. inside the limbus. At places there were gaps, and at the lower part of the ring the dots did not form a well-defined ring. In the oval center were some irregular sizes and shapes, resembling spots of white-lead paint and superficial to Bowman's membrane. The overlying corneal epithelium was smooth.

D. F. Harbridge.

#### 7. UVEAL TRACT, SYMPATHETIC DISEASE, AND AQUEOUS HUMOR

Corrado, M. **The pathogenetic mechanism of detachment of the posterior pigment layer of the iris.** Ann. di Ottal., 1934, v. 62, July, p. 573.

Detachment of the pigment layer of the iris may be the result of trauma either accidental or surgical. The latter is common following iridectomy when marginal synechia is present after an iritis. Removal of the anterior layer has happened in iridectomy in albuminuria, and in diabetes. The morphology in these cases has been little studied. The pigment layer embryologically is the pars iridea of the secondary ocular vesicle. Only in the fifth month is there structural differentiation between the two layers. In cases of primary progressive information a number of observations were made on pathologic globes to demonstrate under various conditions the comportment of the two posterior layers. The author concludes that separation of the layers is favored by congenital lack of firmness of adhesion between the layers.

Park Lewis.

Favaloro, G. **Contribution to knowledge of senile syndromes of the fundus. (Peripapillary choroiditis with optic nerve atrophy and cataract.)** Arch. di Ottal., 1934, v. 41, March, p. 107.

Two patients, eighty-seven and seventy-five years of age, showed peripapillary choroiditis with optic atrophy and cataractous changes. The changes are attributed to senility and arteriosclerosis.

Herman D. Scarney.

Koyanagi, Y. **A case of tuberculous panophthalmitis with special reference to its primary localization.** Klin. M. f. Augenh., 1934, v. 93, July, p. 37.

In a woman of thirty-two years an eye was enucleated after scleral perforation. Tubercle bacilli were isolated in pure culture. From the history and a study of the histologic preparation it is probable that the process had started as an acute tuberculous choroiditis with extensive retinal detachment. Soon afterward the ciliary body and iris became involved. A reactive tissue proliferation failed to check the extension of the tuberculous process.

F. H. Haessler.

Latte, M. **The significance of a normal and a morbid line of droplets on the posterior corneal surface.** Klin. M. f. Augenh., 1934, v. 93, July, p. 29.

Latte outlines the historical development of our knowledge of the line produced on the posterior corneal surface by precipitation of single cells, white blood cells, and pigment cells from the convection currents in the aqueous.

F. H. Haessler.

Palie-Szanto, Olga. **Neosalvarsan in the treatment of sympathetic ophthalmia.** Klin. M. f. Augenh., 1934, v. 93, July, p. 91.

For sympathetic ophthalmia, which she feels is most probably caused by an unknown agent, the author advocates treatment with salvarsan, not an occasional small dose, but in large doses in systematic courses just as in syphilis.

F. H. Haessler.

Strebel, J. **Local and general therapy in sympathetic ophthalmia. A new**

**method for experimental production and therapy of sympathetic ophthalmia.** Klin. M. f. Augenh., 1934, v. 93, July, p. 72.

On the basis of Szily's demonstration that sympathetic inflammation in experimental animals is transferred by way of the ciliary and optic nerves the author injects a one to two thousand solution of mercury oxycyanide directly into the nerve stump of the enucleated eye, and repeats the injections daily. The secondary eye is not injected. The treatment is combined with mercurial inunctions into the forehead and temple and large doses of salicylates. Even more important are considered injection of cyclotropin (urotropin, salicylic acid, caffeine) on the first day. Salvarsan is given for from five to six weeks. If symptoms of intolerance occur one substitutes an injection of amnadin or calcium. The author does not use tuberculin despite his familiarity with it in Sahli's clinic.

F. H. Haessler.

Vannas, Mauna. **On the technique of injection of the patient's blood into the anterior chamber.** Klin. M. f. Augenh., 1934, v. 93, May, p. 662.

After a typical traumatic cataract followed such an injection the author modified his technique. In the side of an ordinary hollow needle he files an opening 8 mm. from the end. This needle is inserted into the anterior chamber near the limbus and the tip is never allowed to cross the pupillary margin, but is directed across the anterior chamber near its periphery and is plunged out at the corneo-scleral limbus at another point on the same side of the pupil as the wound of entrance. The blood can now be safely ejected from the canula. The needle is not withdrawn until clotting has begun.

F. H. Haessler.

Yanes, T. R. **Anterior chamber irrigation.** Rev. Cubana Oto-Neuro-Oft., 1934, v. 3, Jan.-Feb., p. 31.

Irrigation of the anterior chamber for hyphema in the course of an iridectomy for a foreign body in the iris was followed by traumatic cataract. The author feels therefore that irrigation is not



without danger in the presence of a transparent lens, although he admits that working blindly in the presence of hyphema, even without irrigation, might produce the same complication.

M. Davidson.

#### 8. GLAUCOMA AND OCULAR TENSION

Böck, J., Kronfeld, P. C., and Stough, J. T. **Effect on intraocular tension of corneal massage with the tonometer of Schiötz.** *Arch. of Ophth.*, 1934, v. 11, May, pp. 797-806.

The results of studies of the effect of tonometry on normal eyes in fifty persons showed in every case that, after two minutes' application of a tonometer carrying a 15-gm. weight, the tension dropped in proportion to the original tension. Normal eyes with tension between 27 and 32 mm. showed a greater decrease than a small number of glaucomatous eyes having the same original tension. (Tables.) J. Hewitt Judd.

Duke-Elder, W. S. **The etiology of glaucoma.** *Trans. Ophth. Soc. United Kingdom*, 1933, v. 53, pp. 49-57. (See *Amer. Jour. Ophth.*, 1934, v. 17, June, p. 568.)

Hamburger, Carl. **Ten years of glaucoma treatment.** *Klin. M. f. Augenh.*, 1934, v. 93, July, p. 60.

Hamburger reviews ten years' experience with suprarenin and glaucosan. They are most useful for the breaking of adhesions in neglected severe iritis, particularly if one massages the limbus near the synechia with an applicator saturated with the drug. The author also believes glaucosan to be indicated in glaucoma simplex when miotics have failed. After its use they frequently become more effective than before. If a serious rise in tension occurs after glaucosan in glaucoma simplex, in most cases the attack may be aborted rapidly by intravenous injection of 10 c.c. of 10 percent solution of sodium chloride, as suggested by Hertel. The first glaucosan should always be given to a patient in the morning so there will be ample time for observation. After it has been safely given several times an in-

telligent patient may be entrusted with glaucosan at home. Attacks of tension caused by glaucosan are extremely rare in operated eyes. The author never uses glaucosan in both eyes on the same day, even after years of use by that patient. Eyes have also been saved with histamine (amin glaucosan) but it is not reliable nor uniform in its action.

F. H. Haessler.

Liebermann, L. V. **Substitutes for iridectomy? Evaluation of glaucoma operations.** *Klin. M. f. Augenh.*, 1934, v. 92, June, p. 763.

Iridectomy is not an ideal operation without disadvantages. Cyclodialysis can be used in all forms and stages of primary glaucoma, is almost without danger, can be repeated, and can be combined with other operations. It is a method by means of which the aqueous can be drained off without danger of subsequent reaction. The pupil remains round and no astigmatism results.

It is not always effective, at least not permanently. Trephining, of which Elliot's is superior to Lagrange's, can be used for all cases except those in which a reaction is to be expected. Late infection is extremely rare. Basal iridectomy can be more adequately performed than with the usual keratome incision for iridectomy. It can be repeated and combined with cyclodialysis. It leaves a round pupil and no astigmatism. Its disadvantages are the dangers of provoking a malignant reaction (chamber flat, lens blocks the chamber angle, and eye is destroyed by pressure) and later infection.

F. H. Haessler.

Nicolato, A. **Possible causes of deep anterior chamber in primary uncompensated glaucoma.** *Boll. d'Ocul.*, 1933, v. 12, Aug., pp. 721-744.

The writer discusses the pathogenesis of deep anterior chamber in the glaucomatous left eye of a man seventy years old. He thinks that adjustment between the pressure in the anterior and posterior chambers and the reduced outflow of their content as a result of anatomic changes was the cause. Histologic examination of the eye showed,

among other features, that Schlemm's canal and the spaces of Fontana were occluded by exudate in some places, and that in other places the tissue of the angle was changed into connective tissue of the scleral type. (Four tables, bibliography.) M. Lombardo.

Trematore, Mario. **The blood alkalinity in the glaucomatous.** *Lettura Oft.*, 1934, v. 11, April, p. 161.

Tests for alkaline reserve were made on glaucomatous and nonglaucomatous patients. The reserve was a little higher in the glaucoma cases which showed a tendency toward alkalosis.

F. M. Crage.

Tristaino, L. **Arterial pressure, intraocular tension and glaucoma.** *Rassegna Ital. d'Ottal.*, 1934, v. 3, March-April, p. 217.

Tristaino studied three groups of rabbits to determine the relationship between arterial pressure, intraocular pressure, and glaucoma. In the first group the effect of abdominal pressure before and after extirpation of the superior cervical ganglion was studied. An immediate and constant elevation of intraocular tension resulted which averaged 10 mm. and persisted as long as compression was maintained. Upon the side of the extirpated ganglion, there was practically no effect. In the second group, the author studied the effect of abdominal compression before and after instillation of eserine in one eye. This produced a noticeable fall in tension in both eyes. In the third group, the same procedure was followed, instilling atropine in one eye. No apparent effect upon intraocular tension was observed. The author therefore feels that there is a definite relationship between increased general arterial pressure and glaucoma. (Six illustrations.)

Eugene M. Blake.

Vogelsang, K. **On the theory of ballistic measurements of the eye.** *Klin. M. f. Augenh.*, 1934, v. 93, July, p. 26.

With the ballistic elastometer one measures the recoil of a small mass which is projected against the tissue to

be investigated. The technique was first used in studying muscle physiology. In the eye the elasticity measured is one of impression rather than tension. Theoretical conditions are very complex because the recoil is the resultant of the sum of several factors. Conditions are much less favorable in the eye than in muscle.

F. H. Haessler.

## 9. CRYSTALLINE LENS

Almeida, A. de. **Surgery of complicated cataract.** *Arquivos do Instituto Penido Burnier*, 1934, v. 3, March, pp. 42-47.

The author argues that in the absence of ciliary reaction or marked hypotony complicated cataract may always be operated upon. He reports numerous cases of cataract complicated by glaucoma, uveitis, leucoma, and congenital disturbances, and in which the operative result was in general good.

W. H. Crisp.

Borsellino, G. **Experimental endocrine cataract.** *Arch. di Ottal.*, 1934, v. 41, Jan.-Feb., p. 57.

Thyroidectomy in rabbits did not produce lenticular change. After parathyroidectomy there was no manifestation of tetany, no trophic disturbance of the teeth or cutaneous appendages. One result, not constant, was the appearance of small opacities in the crystalline lens principally in the posterior cortical substance. These opacities appeared one month after ablation of the parathyroids, and remained stationary.

Herman D. Scarney.

Burnier, Penido. **Marfan's syndrome and ectopia lentis.** *Arquivos do Instituto Penido Burnier*, 1934, v. 3, March, pp. 20-33.

Four cases of ectopia lentis are reported, making a total of seven cases seen by the author among 61,000 eye cases. Marfan's syndrome (arachnodactylia) coexisted with the ectopia in three of the present four cases.

W. H. Crisp.

Edgerton, A. E., and Fulmer, C. A. **fragment of lens capsule in the ante-**

rior chamber. *Amer. Jour. Ophth.*, 1934, v. 17, Sept., pp. 847-848.

Evans, E. I. **Studies on the crystalline lens.** *Amer. Jour. Ophth.*, 1934, v. 17, Sept., pp. 840-846.

Langston, W. C., and Day P. L. **The arrest of nutritional cataract in the albino rat by the use of vitamin G (B2).** *Southern Med. Jour.*, 1934, Feb., p. 170.

Young albino rats were kept on a vitamin G-deficient diet for forty-two days, by which time most of them had developed incipient cataract. Varying amounts of milk powder containing vitamin G were then added to the food. Amounts of 0.1 gm. or more of milk powder per day prevented the cataracts from maturing in seventy-five percent of the cases. Amounts of 0.05 gm. or less per day retarded the development of the cataracts but did not prevent them from maturing. No curative effect of the vitamin was noted.

John C. Long.

O'Connor, Roderic. **Cataract extraction by the undetached conjunctival bridge method after preliminary iridectomy.** *Amer. Jour. Ophth.*, 1934, v. 17, Sept., pp. 809-817.

Rones, B. **Anterior lenticonus.** *Jour. Amer. Med. Assoc.*, 1934, v. 103, Aug. 4, p. 327.

From a study of the literature and the author's case it is concluded that anterior lenticonus is probably the result of congenital or acquired disturbance of the pressure relationships in the lens system. The congenital form bears no relationship to delayed separation of the lens vesicle from the surface ectoderm. The anomaly here presented appeared to be the forerunner of the congenital type of anterior lenticonus, though the possibility of disappearance of the fluid and ingrowth of normal lens fibers must be borne in mind. Since the anomaly is present prior to development of the hyaline capsule and the zonular fibers, it is apparent that the underlying cause of congenital lenticonus is not a deficiency in these structures. (Four figures, discussion.)

George H. Stine.

Rones, B. **The Wilmer iridocapsulectomy.** *Arch. of Ophth.*, 1934, v. 11, June, pp. 976-981.

The conjunctiva is incised 7 mm. from the limbus and the flap dissected down to the limbus. A catgut suture is placed at each corner to permit rapid closure. With an Agnew spade knife, an incision is made beneath the conjunctival flap at the limbus, and then the knife is plunged through the iris into the vitreous until the resultant incision is the full width of the knife, 5 mm. From each end of the horizontal incision a convergent cut is made downward with a de Decker or a berens scissors, thus removing a triangular section with the apex below. The procedure attempts to assure maximum operative speed plus measures of safety, and to avoid traction on the ciliary processes with ensuing iridocyclitis or glaucoma. The operative steps are well shown by drawings.

J. Hewitt Judd.

Semadini, Bernardo. **Fractional radiation of the rabbit's iris, with remarks on Goldmann's burning of the iris and his alleged heat cataract.** *Klin. M. f. Augenh.*, 1934, v. 92, June, p. 779.

The author believes that Goldmann's irradiation produced actual overheating and iris burns, to which the resulting cataract was secondary in the sense of cataracta complicata. He used apparatus similar to Goldmann's and subjected the iris to many hours of irradiation without direct irradiation of the lens and without injury to iris or corneal tissue. The lens never became cataractous. This work supports Vogt's view that penetrating ultrared rays are the cause of glassblower's cataract.

F. H. Haessler.

Shapira, Thomas. **Suction in extraction of soft cataracts.** *Klin. M. f. Augenh.*, 1934, v. 92, June, p. 768.

For extraction of soft cataract, of the clear lens in myopia, and of partial cataract, suction of the soft masses after preliminary discission is practiced at the Prague clinic. The chamber is opened with a keratome incision 5 mm. long. If the lens capsule has not been opened by preliminary discission, this



is done with the keratome. A canula with rubber tube is introduced and suction is applied by mouth. The iris remains in place throughout the procedure. In three of one hundred and thirty operations, enough fluid vitreous was sucked out to cause collapse of the eyeball, but the end result was satisfactory.

F. H. Haessler.

Thiel, R. **Sunflower cataract with hepato-lenticular degeneration (pseudosclerosis)**. *Klin. M. f. Augenh.*, 1934, v. 93, July, p. 12.

In a fifteen-year-old boy with extrapyramidal motor disturbances the disease started with spasms of the facial musculature, and tonic contraction of the entire musculature later occurred spontaneously and with voluntary movements. The intellect was normal but there were strikingly rapid changes of mood. A severe liver lesion was demonstrable. Under the lens capsule was a delicate opacity presenting the picture of a sunflower. There was a striking yellow discoloration and iridescence in the region of the opacity. These findings are also characteristic of chalcosis. There was also a typical yellowish-brown pigment ring on Descemet's membrane. Sufficient data were not at hand to permit conclusion as to the nature of the pigment.

F. H. Haessler.

Villano, G. **Vossius cataract**. *Rassegna Ital. d'Ottal.*, 1934, v. 3, March-April, p. 235.

The author describes a second case of Vossius cataract in an eleven-year-old girl, following a blow on the left eye from a stone. He discusses the various explanations offered by different writers as to pathogenesis. His own feeling is that the cataract is a slight transitory commotio of the anterior superficial layer of the lens following an external blow, transmitted through the cornea and aqueous to the pupillary margin of the iris. There is thus produced an impressed design of the pupillary margin of the lens. (One illustration.)

Eugene M. Blake.

Yanes, T. R. **Ocular tension in cataract extraction**. *Rev. Cubana Oto-Neuro-Oft.*, 1934, v. 3, Jan.-Feb., p. 7.

Attention is called to the importance of knowledge of ocular tension in cataract operations. In low tension there is a tendency of the lens to sink backward and there is no risk of vitreous presentation. Simple extraction is indicated. If the tension is below normal it should be elevated to 20 mm. (McLean) by atropin or one can wait for its spontaneous elevation to normal. Higher tension even if within normal limits predisposes to iris prolapse and presentation of lens and vitreous; and combined extraction is indicated.

M. Davidson.

#### 10. RETINA AND VITREOUS

Ariani, Paulo. **Retinal endarteritis**. *Arquivos do Instituto Penido Burnier*, 1934, v. 3, March, pp. 57-61.

The author reports a case of sudden loss of vision from endarteritis of the upper temporal branch in a woman of twenty years. Removal of some dental foci, together with protein therapy, failed to change the condition; but, following a positive Wassermann test, intramuscular administration of bismuth and ocular ionization with sodium iodide led to rapid recovery.

W. H. Crisp.

Arruga, H. **The development of retinal tears and of idiopathic retinal detachment**. *Klin. M. f. Augenh.*, 1934, v. 93, July, 43.

If we ignore those cases of retinal detachment caused by tumor, parasites, and choroidal exudate, which usually have no retinal dehiscence, and those following postoperative vitreous traction, we have left the idiopathic detachments, in the majority of which a tear can be found. In these the retina is abnormal. If the normal retina is incised as in sclerotomy the retinal edges become applied to the choroid and heal without detachment. If the retina is normal it may become detached by an exudate but returns to its normal position when the exudate is removed. Two types of lesion are found in enu-

cleated eyes with freshly detached retina: vascular degeneration and atrophy. Sometimes one sees remains of the vitreous framework adherent to the retina in the zone of detachment. After scleral irritation, whether chemical or thermal, similar adhesions are formed. Another factor of great importance is retraction of the sclerosed retina. The retina like any other tissue shrinks when atrophy or sclerosis follows a degenerative or postinflammatory change. Because of its delicacy, which is even greater in vascular degeneration, a retinal dehiscence may result from this shrinkage. Trauma to the eye or even concussion of the skull may initiate such a tear.

F. H. Haessler.

Arruga, H. **Immobilization of the eyeball in the treatment of retinal detachment.** *Klin. M. f. Augenh.*, 1934, v. 93, July, p. 52.

The author found that the suture suggested by him, even when ideally placed through the tendon of the inferior rectus and the tarsus of the lower lid, produced immobility for only three or four days. Now he uses a retrobulbar injection of 5 to 9 c.c. of the patient's own blood. This immobilizes the eyeball for two to three days and must be repeated. The addition of one drop of 90 percent alcohol or 1 to 1000 solution of mercury cyanide to each c.c. of blood increases its time of effect even up to several weeks, but eventually mobility always returns perfectly. Various blood coagulating substances added to the blood were of no help.

F. H. Haessler.

Busacca, Archimede. **Neuroretinitis from the use of hair dye; with macular star.** *Folia Clinica et Biologica*, 1934, v. 6, April, pp. 45-49.

A woman of forty-seven years had noticed progressive failure of vision of the left eye for about two months. She had been using a hair dye for two years, and had a well developed eczema of the hairy scalp. The right eye had corrected vision of one-fourth, and the disc presented the picture of hypermetropic pseudoneuritis. The left eye had vision

of one-eighth unimproved with lenses. The posterior pole of the left fundus was decidedly edematous, and the disc had typical signs of neuritis. There were four round hemorrhages in the area between the superior and inferior nasal vessels. Recovery followed withdrawal of the dye, and internal use of sodium salicylate, iodine, and sulphur. The disturbing effect was apparently due to acetate of lead.

W. H. Crisp.

Cordero, C. **Experimental researches on adhesive chorioretinitis from diathermocoagulation.** *Arch. di Ottal.*, 1934, v. 41, Jan.-Feb., p. 65.

The first group of rabbits' eyes was treated by diathermy puncture; the second group was treated by surface application of the diathermy electrode. The eyes were enucleated at intervals varying from fifteen hours to seventy days, and were examined histologically. The tissue reaction was less after the perforating technique. The canal caused by perforation was healed in from sixty to seventy days. The cases treated by superficial diathermy showed extensive repair processes beyond the point of treatment, with intense iritis, cyclitis and clouding of the vitreous.

Herman D. Scarney.

Galeazzi, C. **Cholesterinemia and cataract.** *Rassegna Ital. d'Ottal.*, 1934, v. 3, March-April, p. 199.

Starting from the facts deduced by Vollaro in his studies of the morphological syndromes of the cholesterinized steatitis of the normal eye, Galeazzi determined the amount of cholesterol in the blood of forty-five individuals with cataract. He obtained an average value which corresponds closely to the normal (0.177 percent). He concludes that senile cataract may result from exaggeration of a physiological condition, namely, infiltration of the senile lens with cholesterinized esters, especially in conditions of hypercholesterinemia. This is especially apt to occur when there is altered permeability of the lens capsule with lessened selective power of the capsular epithelium.

Eugene M. Blake.

Junius, Paul. **On the etiology of retinitis exudativa of Coats.** *Klin. M. f. Augenh.*, 1934, v. 92, June, p. 748.

The author presents a review of the recent literature on retinitis exudativa and concludes that we are justified in considering it a clinical entity. He points out the importance of recent dermatological work on generalized angiomatosis (teleangiectasis.) Miliary aneurisms and less visible changes (possibly physico-chemical) in the minute vessel walls probably play an important rôle in the genesis of retinitis exudativa.

F. H. Haessler.

Kraupa, Ernst. **The development of vitreous vascular proliferations with senile retinal vessels.** *Klin. M. f. Augenh.*, 1934, v. 93, July, p. 70.

One retina observed indicated that primary proliferation of the retinal vessels into the vitreous does not occur. These vessels leave the optic nerve and retina only when the limiting membrane becomes detached. Just as there are preretinal hemorrhages, exudations, and precipitates so there are preretinal vascular proliferations which are separated from the vitreous by its limiting membrane until this membrane (whose existence Kraupa has demonstrated) becomes detached and torn.

F. H. Haessler.

Krause, A. C. **Chemistry of the vitreous. 1, Chemical composition of the proteins.** *Arch. of Ophth.*, 1934, v. 11, June, pp. 960-963.

The amount and distribution of nitrogen in the mucoid and residual protein or vitrein were determined in the vitreous of the ox eye by the Van Slyke method. The distribution of the basic amino-acids was calculated from the Van Slyke method and the colorimetric method of Folin and Marenzi. The author concludes that the distribution of the vitrein suggests that the vitreous is not a uniform gel and that the hyaloid membrane is not a condensation but is composed of vitrein, which is closely related chemically to the zonular fibers and the lens capsule.

J. Hewitt Judd.

Krause, A. C. **Chemistry of the vitreous humor. 2, Proteolysis.** *Arch. of Ophth.*, 1934, v. 11, June, pp. 964-968.

Experiments were conducted to determine the results of autolysis of the vitreous of bovine eyes, alone and after the addition of white blood cells, at the normal pH of 7.5, and when acidified to the pH of 6.5. Krause concludes that vitreous may lose its turgidity through loss of mucoid at the normal pH in the presence of white blood cells, which produce heterolysis through the proteolytic enzymes they contain. Liquefaction, produced by decrease of the vitrein and mucoid, may result from an abnormal increase in the hydrogen-ion concentration of the vitreous.

J. Hewitt Judd.

Lijo Pavia, J. **Capillaritis of the fundus.** *Rev. Oto.-Neuro-Oft.*, 1934, v. 9, June, p. 204.

Apropos of a diagnostic error observed and of Bailliar's work, the use of red-free ophthalmoscopy, binocular ophthalmoscopy, biomicroscopy of the fundus and blood chemistry is stressed.

M. Davidson.

Lijo Pavia, J. **Evolution of a patch of green color and foci of capillaritis.** *Rev. Oto.-Neuro-Oft.*, 1934, v. 9, May, p. 154.

Previous studies indicate that the greenish color seen in fundus lesions is due to presence of blood serum in the retinal or choroidal tissues. In the case of diabetic chorioretinitis now reported, fluctuations in the green coloration of the same lesions accompanied fluctuations of the blood-sugar content, increasing with it. The conversion of bilirubin into biliverdin is assumed to give rise to the greenish coloration. (Illustrated.)

M. Davidson.

Lijo Pavia, J. **Further observations of "green patches in the fundus."** *Rev. Oto.-Neuro-Oft.*, 1934, v. 9, July, p. 227.

A new case is reported of "green" focus and of atrophic retinal lacuna. By means of stereoscopic retinographs, the first was localized in the choroid and the latter in the external retinal layers.

M. Davidson.



Lijo Pavia, J. **Striking changes from diathermy for retinal tear in a case of severe diabetic chorioretinitis.** *Rev. Oto-Neuro-Oft.*, 1934, v. 9, April, p. 126.

In a diabetic woman of fifty years, with one eye blind and the other, as a result of a head contusion, the seat of a horizontal macular tear on top of a marked chorioretinitis, with light perception only, diathermy was resorted to. Two special devices had to be used in this difficult case. Glass rods with prongs at the ends, to hold back and grasp the optic nerve, and with holes at 4, 5, and 6 mm. from the base of the prongs, for passage of the diathermic needle, were utilized. The other device was simultaneous use of the Lange transilluminator and ophthalmoscopy, made possible by a contact glass, to mark accurately the site of the puncture on the sclera. After twenty-nine days the chorioretinal exudates had been sufficiently absorbed to permit identification of the papilla and numerous vessels near the site of the puncture, either retinobulbar anastomoses or new-formed vessels and some hemorrhagic spots. Vision was improved to 1/16, and there was marked improvement in the fields.

M. Davidson.

Lijo Pavia, J. and Dusseldorp, M. **The effect of sympathectomy on a case of postanemic fundus changes.** *Rev. Oto-Neuro-Oft.*, 1934, v. 9, May, p. 164.

Sympathectomy on the left side was attempted in a woman blind for eight years after severe bleeding. The right disc was atrophic, the left disc pale pink with cystoid degeneration of the macula and a yellow bridge between disc and macula. There was improvement in vision from 1/100 to 1/60 in the right eye and from 1/60 to 1/10 in the left eye, considerable recovery of fields, some disappearance of pigmentation between macula and papilla on the left side, and, with red-free light, less marked cystoid degeneration of the macula and disappearance of the bridge seen before.

M. Davidson.

Lijo Pavia, J., and Dusseldorp, M. **Retinitis pigmentosa with macular changes.** *Rev. Oto-Neuro-Oft.*, 1934, v. 9, April, p. 118.

A rare case of combination of equatorial and macular lesions in a male of fifty years, without consanguinity in the family history, is described and illustrated with fundus photographs. Greenish discoloration of the choroidal intervascular spaces, noted ophthalmoscopically and visible in color photographs, is interpreted to indicate hyalin thickenings of the vessel walls. Central macular lesions are considered as defects in the external and pigment layers of the retina. Hepatic extract improved vision, color sense, and dark adaptation.

M. Davidson.

Lijo Pavia, J., and Dusseldorp, M. **Unusual medullated nerve fibers.** *Rev. Oto-Neuro-Oft.*, 1934, v. 9, July, p. 233.

Two cases of unusual extent of medullation are described, confined to one eye in each case.

M. Davidson.

Lissner, H. H. **Magnesium sulphate—its intravenous use in hypertension and allied eye conditions.** *California and Western Med.*, 1934, v. 40, May, p. 330.

Intravenous injection of magnesium sulphate solution has a distinct palliative effect in reducing vascular hypertension and its symptoms, but the pressure resumes its original high level after the drug has been discontinued. Intravenous injection of magnesium sulphate apparently lowers intraocular tension, aids absorption of retinal exudates, and makes hypertensive retinal changes less likely to occur.

John C. Long.

Meding, C. B. **Free cyst floating in the vitreous.** *Arch. of Ophth.*, 1934, v. 11, June, pp. 973-975.

For seven months a woman of forty-two years had noticed a "black ball" passing before her right eye. A spheroid, pigmented, translucent, lens-size cyst was found just posterior to the lens. It moved freely but seemed to be confined to a circumscribed shallow area. The author suggests that the cyst

had existed since birth but had been as transparent as the vitreous up to the date of its interference with vision. Previously reported cases are summarized in a table. (Drawing.) J. Hewitt Judd.

Mossa, G. **Experimental retinitis proliferans.** *Rassegna Ital. d'Ottal.*, 1934, v. 3, March-April, p. 272.

Mossa injected from a quarter to a half c.c. of blood into the vitreous of rabbit eyes. Hemorrhagic retinitis resulted only when the retina was directly injured, but neither with the ophthalmoscope nor histologically was there any picture corresponding to proliferating retinitis. Eugene M. Blake.

Niccol, W., and Moore, R. F. **A case of angiomas retinae.** *Brit. Jour. Ophth.*, 1934, v. 18, Aug., p. 454.

A man aged thirty-two years had passed a flying test as pilot two years previously. He had noticed a black spot before his vision after an attack of influenza, fourteen days before being seen, and for the last five days had been troubled by metamorphosia. The left eye was normal, the right had vision of 6/36. The visual field showed an enlarged blind spot toward fixation. Ophthalmoscopically, adjoining and overlapping the temporal edge of the papilla was an irregular raspberry-like formation. The general color was slate-grey, portions being reddish or purplish. Rucking of the retina was present between the mass and the macula, and subsequently a small shallow detachment of the retina was observed in this area. In discussion it was suggested to use radon seeds, but a third surgeon believed that, in view of possible malignancy, it would be wiser to remove the eye. (Four illustrations.)

D. F. Harbridge.

Rice, C. O. **An unusual case of pigmentation of the retina.** *Amer. Jour. Ophth.*, 1934, v. 17, Sept., p. 847.

Rötth, A. **A model to demonstrate the mechanism of retinal detachment.** *Klin. M. f. Augenh.*, 1934, v. 93, July, p. 47.

Rötth has developed a model to show how active traction in the vitreous may

bring about a retinal tear with consequent retinal detachment. He lines a one-liter Florence flask with a 2-mm. layer of gelatine and to this attaches a silk thread at two diametrically opposite points on the equator. A thin layer of rubber cement in benzine is added and finally a layer of celloidin. When all is dry the flask is filled with water and the flask rotated in a jerky manner until a tear develops in the lining. The point of the tear usually develops toward the papilla, as is the case in many retinal detachments. The author offers these experiments in support of the theory that retinal detachment results from myopic senile degeneration of the peripheral retina and vitreous; the vitreous then causing traction on the area between equator and ora serrata, which is normally most firmly adherent. F. H. Haessler.

Safar, K. **Detachment of the retina. Treatment with multiple diathermic puncture and its results.** *Arch. of Ophth.*, 1934, v. 11, June, pp. 933-941.

Multiple punctures of the sclera are made with single or multiple diathermic needles 1.8 mm. long in the area surrounding the tear, causing coagulation of the underlying choroid. The needles are not removed until all are in place. After removal, the subretinal fluid escapes through the punctures, the retina comes in contact with the choroid, the tear is sealed by the chorioretinal adhesions, and the detachment of the retina is healed. Various types of electrode are described and illustrated. A frequency of 30,000 to 50,000 is best as it allows easy perforation of the sclera, with moderate coagulation. The strength of current used is from 30 to 50 ma. for an electrode having one needle, from 80 to 100 ma. for an electrode with three needles, and from 150 to 200 ma. for one with five to eight needles. The author reports permanent reattachment of the retina with good vision and restoration of the visual field in 57.5 per cent of forty unselected cases in 1932 and in 85 per cent of the first forty eyes operated on in 1933. (Drawings.)

J. Hewitt Judd.

Schlesinger, B., Greenfield, J. G., and Stern, R. O. **A case of late infantile amaurotic idiocy.** Arch. Dis. in Childhood, 1934, v. 9, Feb., p. 1.

A late infantile form of amaurotic idiocy is reported in a Gentile female. The child appeared normal until the age of ten months. Progressive mental deterioration and generalized spastic paralysis developed. Ocular findings were sluggish pupillary reactions to light, variable external strabismus, and bilateral primary optic atrophy. No macular changes were noted. Death occurred at twenty-two months. Very elaborate neuropathological studies were made. Extensive lipid deposits were found in the nerve cells throughout the central nervous system. A general discussion of the disease is included. Amaurotic family idiocy and Niemann-Pick disease are both regarded as different manifestations of the same condition. John C. Long.

Seech, S. G. **Congenital cyst in the vitreous.** Arch. of Ophth., 1934, v. 11, June, pp. 947-949.

The previously reported cases are summarized. The author reports the case of a woman of twenty-three years, with compound myopic astigmatism, who complained of intermittent blurred vision of the left eye of a few seconds duration. A translucent oval cyst was seen moving freely in the center of the lower half of the vitreous. There was considerable black pigment at several places on the inner surface of the cyst. The fundi were normal. Since there was no evidence of intraocular inflammation or degeneration, the cyst was thought to be developmental rather than pathologic. J. Hewitt Judd.

Stokes, W. H. **Racemose arteriovenous aneurism of the retina.** Arch. of Ophth., 1934, v. 11, June, pp. 956-959.

This rare anomaly was found during routine examination in the left eye of a girl of ten years, with normal vision. The anastomosis and marked dilatation of the vein are well shown by a colored plate. Seven similar cases found in the literature are summarized.

J. Hewitt Judd.

Vogt, Alfred. **Cystoid degeneration of the retina and its accompanying linear networks, as well as the optical condition under which the cysts become visible.** Klin. M. f. Augenh., 1934, v. 92, June, p. 743.

Large macular cysts may be mistaken for holes, but the anterior wall is visible in redfree light. In the periphery, it is difficult to use redfree light, though with the indirect method he saw peripheral cysts in retinal detachment in 1927. When the retina becomes reattached, the cysts disappear because the light is reflected from the choroid. The differentiation is important because holes must be closed surgically while cysts may be left.

The network of white lines which is often seen ophthalmoscopically in peripheral cystoid degeneration of the retina represents obliterated blood vessels. If they are followed centrally their junction with patent vessels can be found.

F. H. Haessler.

#### 11. OPTIC NERVE AND TOXIC AMBLYOPIAS

Adler, F. H. **Apparent optic atrophy with recovery of normal central visual acuity.** Arch. of Ophth., 1934, v. 11, June, pp. 942-946.

In a man of thirty-eight years vision was gradually reduced to light perception in each eye after six injections of tryparsamide. There was apparent complete atrophy of both discs with contracted and tortuous retinal arteries. The visual fields were markedly contracted. The patient was treated with strychnine and the sinusoidal current. After one year the central vision was essentially normal and central color vision was recovered. The fields remained contracted to the point of fixation. The temporary loss of central vision was attributed to "physiologic block." The lesion was thought to be in that part of the optic nerve at which the macular fibers leave their central position. The medicolegal importance of differentiating between optic atrophy due to the toxic action of tryparsamide and that due to early tabes is stressed.



In true tabetic atrophy the vision never returns when once lost.

J. Hewitt Judd.

Andrade, C. de. **Two cases of hemi-craniosis with optic atrophy.** *Rev. de Ophth. de São Paulo*, 1934, v. 3, June, pp. 225-229.

In the first case there was considerable thickening of almost the whole left frontoparietal wall, particularly near the base, and between the pterygoparietal, coronary, and sagittal sutures. The eye on the same side protruded and showed rhythmic movements. The vision of this eye was limited to one third, with a four-diopter correction. There was a pyriform tumor (molluscum) on the left side of the face, beginning at the zygomatic arch. The atrophy of the optic nerve was regarded as due to compression in the optic canal. The second case was similar, but with complete atrophy of the left optic nerve and greatly reduced hearing on the same side.

W. H. Crisp.

Carreras, J. L. **Optic nerve and acetylarsan.** *Rev. Oto-Neuro-Oft.*, 1934, v. 9, June, p. 209.

Among 8,534 injections no ocular complications have been observed and acetylarsan is considered the least toxic of the pentavalent arsenicals.

M. Davidson.

Grimsdale, Harold. **A case of gas-poisoning with unusual ophthalmological complications.** *Brit. Jour. Ophth.*, 1934, v. 18, Aug., p. 443.

A sewer man aged thirty-two years went into a sewer into which passed the effluent from a sulphate of ammonia plant, which was being flushed with a stream of boiling water. He was brought to the surface unconscious. His right arm was severely scalded. Artificial respiration was instituted. He remained in a coma four days, made no effort to swallow, and had no control over excreta. Five days later he seemed quite blind, paying no attention to a bright light, but the pupils reacted well and the fundi were normal. About three months later the light perception field had markedly improved. The last notes,

nine months later, showed color perception seemingly better relatively than light perception. The fundi remained normal, discs good color. Three similar case reports in the literature are referred to. It is rare for gas poisoning to be followed by so many serious symptoms.

D. F. Harbridge.

Klauber, E. **Treatment of optic nerve lesions with sodium thiosulphate glucose.** *Klin. M. f. Augenh.*, 1934, v. 92, June, p. 803.

The author injects intravenously one gram of sodium thiosulphate in ten c. c. of a thirty percent glucose solution at intervals of one or two weeks for ten treatments. It is simple and harmless, and in one case of retrobulbar neuritis briefly reported improvement followed its use. In two cases of advanced tabes he thinks that similar injections retarded the disintegration.

F. H. Haessler.

Mazzi, L. **Action of acetylcholine in amblyopia and amaurosis from quinine.** *Arch. di Ottal.*, 1934, v. 41, Jan.-Feb., p. 27.

Two dogs were given large doses of quinine subcutaneously. Both animals developed quinine amaurosis. Several months later one eye was enucleated from each animal and studied histologically; and, several days after the enucleation, each animal was given an injection of 5 cg. of acetylcholine chloride for eight successive days. After these injections there was miosis with moderate retinal hyperemia. The author attributes the amaurosis after quinine to the direct action of the alkaloid on the nervous elements of the retina, and regards the vasoconstriction as secondary. The injections of acetylcholine gave no improvement in vision.

Herman D. Scarney.

## 12. VISUAL TRACTS AND CENTERS

Drouet, P.-L., Jeandelize, P., and Gault, A. **A study on the modifications of the visual field in the hyperthyroid syndrome and para-Basedowism.** *Ann. d'Ocul.*, 1934, v. 171, June, pp. 465-479.

Beside the usual form of hyperthyroidism there exists a slightly different

condition, here termed para-Basedowism. There are many of the cardinal signs of hyperthyroidism, such as tachycardia and tremor, but the basal metabolism remains normal. An instability of the sympathetic nervous system is the explanation for this second condition. Many eye findings are common to both.

Of eleven cases of hyperthyroidism over half showed a bitemporal field defect. Melanin was found in the urine in these cases, confirming the impression of pituitary disturbance. Three out of four cases of para-Basedowism showed the same melanin and field changes. The conclusion is that the pituitary gland is hyperplastic and overactive.

H. Rommel Hildreth.

Garvey, P. H. **Aneurisms of the circle of Willis.** *Arch. of Ophth.*, 1934, v. 11, June, pp. 1032-1054.

Stressing the clinical symptoms and signs which lead to their recognition during life, the author reviews briefly the clinical and pathologic features in aneurismal dilatations involving the vessels of the circle of Willis. He reports the clinical findings and pathologic changes in four cases, and the clinical findings in a fifth case. In cases one and two the diagnosis of intracranial aneurism was verified at necropsy. In cases three and four clinical diagnoses of meningovascular syphilis and cerebral tumor, respectively, had been made. The fifth patient is still living, but the findings are similar to those of cases one and two, and the course has been sufficiently characteristic to warrant a diagnosis of intracranial aneurism.

J. Hewitt Judd.

Phillips, Gilbert. **Perception of flicker in lesions of the visual pathways.** *Brain*, 1933, v. 56, Dec., p. 464.

The author describes an apparatus for testing the perception of flicker in various portions of the visual field. Size and intensity of the flickering area, light adaptation, and adaptation to flicker must be kept constant. Flicker perception in lesions of the chiasm was studied. Flicker perception is diminished on the involved side and may be

diminished in the absence of any visual field defect. The flicker perception defect appears in some degree in all quadrants in cases of chiasmal compression. A few patients with suprachiasmal lesions were studied. Flicker perception may be diminished in one or both contralateral half fields in the absence of any defect for form. It is suggested that there may be a dissociation between flicker perception and form-movement perception.

John C. Long.

Silva, L., and Elejalde, P. **Ocular manifestations of luetic basal meningitides.** *Annaes de Ocul. do Rio de Janeiro*, 1933, v. 5, no. 3, pp. 11-26.

In some detail, and with numerous illustrations, the authors describe three cases of basilar meningitis. In the first case the oculomotor nerves were only involved on one side. In the second case a convulsive apoplexy was followed by paralysis of the third, fourth, and fifth nerves. Antiluetic treatment led to complete cure. The third patient had a gumma in the region of the right half of the chiasm, pressing upon the trochlear nerve and optic tract, and also upon the hypothalamus. Antiluetic treatment rapidly produced marked improvement.

W. H. Crisp.

### 13. EYEBALL AND ORBIT

Kraupa, E. **Cartilage implants from the calf after enucleation.** *Klin. M. f. Augenh.*, 1934, v. 93, May, p. 666.

Kraupa finds the prepared cartilage masses for implantation to be sterile, and to heal into the tissues satisfactorily. Lowenstein's sutures into the depth of the orbit prevent extrusion.

F. H. Haessler.

Salit, P. W. **Chlorine content of aqueous, vitreous, and serum.** *Amer. Jour. Ophth.*, 1934, v. 17, Sept., pp. 818-819.

Sorsby, Arnold. **Anophthalmos: An unpublished manuscript by James Briggs giving the first account of the familial occurrence of the condition.** *Brit. Jour. Ophth.*, 1934, v. 18, Aug., p. 469.

The unpublished MS. is at the library of the Royal College of Surgeons. In a

family of seven, three children were born with total absence of both eyeballs. In the fourth there was total absence of one eyeball and its fellow was greatly malformed. The opening between the lids admitted a crow's quill. Tarsal cartilages, lacrimal glands, and the membrane lining the lid which terminated toward the posterior part of the orbit were all present. At the age of three years the malformed eyeball had increased in growth with the rest of the body, the cornea however being less than one-fourth of an inch in diameter. At the age of thirteen years, there was some light perception.

D. F. Harbridge.

#### 14. EYELIDS AND LACRIMAL APPARATUS

Biro, Emmerich. **On two cases of acute dacryoadenitis.** *Klin. M. f. Augenh.*, 1934, v. 93, May, p. 664.

Acute dacryoadenitis is one of the rarer affections. In two cases a tender swelling occurred in the characteristic location. The region became edematous, the preauricular gland swollen, and the eyeball displaced. The pus sought an outlet through the skin, instead of through the conjunctiva as is usually described.

F. H. Haessler.

Dusseldorp, M. **Resection of the orbicularis for spastic entropion.** *Rev. Oto-Neuro-Oft.*, 1934, v. 9, June, p. 207.

Resection of the orbicularis of the lower lid is indicated in most cases and should be more often resorted to. No relapses and no secondary ectropion have been observed after the procedure.

M. Davidson.

Friedman, R., and Wright, C. S. **Phthiriasis palpebrarum. Report of a case.** *Arch. of Ophth.*, 1934, v. 11, June, pp. 995-997.

A nineteen-year-old boy had blepharitis of the right eye. Numerous ova were found on the cilia and the right eyebrow, and examination revealed pediculosis pubis. Ova were also found on hairs about the umbilicus, on the sternum, in both axillae, and on both thighs. Photographs show the condition

of the lids and a cilia with ovum attached.

J. Hewitt Judd.

Gowen, G. H. **Newer knowledge of bacteriology applied to ophthalmology.** *Amer. Jour. Ophth.*, 1934, v. 17, Sept., pp. 820-825.

Lindner, K. **The ptosis operation of Blaskovics.** *Klin. M. f. Augenh.*, 1934, v. 93, July, p. 1.

Lindner thinks the Blaskovics operation entirely satisfactory. It avoids the cosmetic defect of the Hess operation and the diplopia which sometimes follows a Mota's operation. It is difficult to repeat the operation on the same eye but this is seldom necessary. Lindner follows Blaskovics' technique, which was adequately described in the *Archives of Ophthalmology*, 1923, volume 52, page 563. Lindner's illustrations are superior and should be consulted.

F. H. Haessler.

Mazzi, L. **Bilateral facial coloboma with oculopalpebral adhesion and ocular complications.** *Arch. di Ottal.*, 1934, v. 41, March, p. 148.

The patient had linear scars on the upper lip over the canine teeth, and in the naso-facial folds extending to the internal canthus there were dense fibrous cords. There were adhesions between the globe and the defective portion of the lower lid at the internal canthus. Both lower puncta were absent, and on the right side there was a small fistulous opening opposite the ala of the nose. Both corneas showed nebulae. (Photographs.)

Herman D. Scarney.

Peer, L. A. **Repair of coloboma of the upper eyelid.** *Arch. of Ophth.*, 1934, v. 11, June, pp. 1028-1031.

The author describes, and illustrates by drawings and photographs of a case, an operation for repair of a coloboma not centrally located, and not extending far above the upper border of the tarsus. The skin of the adjacent lid was dissected free, turned down trapdoor fashion, and sutured with the skin toward the globe. One week later the denuded area was covered by a free, full-thick-



ness skin graft from the opposite upper eyelid. A small residual notch was repaired by a procedure similar to the Blair-Mirault operation for harelip.

J. Hewitt Judd.

# 15. TUMORS

DeLong, Perce. **Primary tumors of the optic nerve.** Amer. Jour. Ophth., 1934, v. 17, Sept., pp. 797-800.

Mazal, Vladimir. **Corneal carcinoma.** Ceskoslovenska Ophthalmologie, 1933, v. 1, no. 3, pp. 147-149.

On the cornea of a seventy-year-old man, whose eye had been injured seventeen years earlier, a 9 by 7-mm. tumor developed. It extended from the limbus at four o'clock and reached its greatest diameter toward the center of the cornea. The tumor was removed and the cornea cauterized. According to the history the tumor developed not at the limbus but from the cornea proper. The diagnosis of carcinoma was confirmed by histologic examination.

G. D. Theobald.

Petri, M. de. **Sarcoma of the choroid and glaucoma.** Boll. d'Ocul., 1933, v. 12, Aug., pp. 770-787.

The tumor was on the nasal side of the fundus, with extensions through the sclera around the optic nerve. It was a small round-cell and spindle-cell sarcoma. The author attributes the increased intraocular tension not so much to the size of the tumor but to compression and closure of the choroidal blood vessels by the tumor. (Bibliography, seven figures.)

M. Lombardo.

Pincus, L. **Cylindroma of the lacrimal gland and trauma.** Klin. M. f. Augenh., 1934, v. 93, May, p. 660.

A boy of fourteen years collided with a plank, whereupon a hemorrhage occurred in the lids. A tumor developed and upon excision was found to be a cylindroma. Bulbar movements were limited up and temporally. In nine similar cases reported in the literature trauma is a probable cause of development of the neoplasm.

F. H. Haessler.

Rand, C. W. **Glioma of the retina. Report of a case with intracranial extension.** Arch. of Ophth., 1934, v. 11, June, pp. 982-994.

The author reviews the literature and reports the case of a girl aged four years, in whom enucleation was not performed until two years after the first symptom. The cut end of the nerve showed the presence of tumor cells. There was rapid local recurrence in spite of intensive roentgen therapy. Intracranial resection of the optic nerve, six months later, showed that the tumor had already invaded the chiasm and the base of the brain. Death ensued in one month from basal meningitis. The author pleads for early enucleation, careful examination of the nerve section, and, where the tumor has extended intracranially, resection of the nerve from the chiasm outward. (Photomicrographs.)

J. Hewitt Judd.

Sgrosso, S. **Concerning hamartoma of the lacrimal caruncle.** Arch. di Ottal., 1934, v. 41, Jan.-Feb., p. 90.

A tumor the size of a pea at the internal canthus of the left eye, occupying the site of the lacrimal caruncle, is described. It was associated with microphthalmos of the same eye. The growth was removed completely without removal of the microphthalmic globe. Histologic examination revealed epithelial structure with sebaceous glands, cilia, smooth muscle fibers, and much adipose tissue.

Herman D. Scarney.

Sisson, R. J. **Lymphosarcoma invading the orbit.** Jour. Michigan State Med. Soc., 1934, v. 33, Jan., p. 21.

The patient was a man of fifty years. By Kroenlein's approach a tumor was removed from near the apex of the muscle cone. After pathological report of lymphosarcoma, the orbit was exenterated. An erosion of the inferior orbital plate and of the lateral ethmoidal wall was treated by x-ray. The patient was quite well eight years after the exenteration was done.

John C. Long.

Sobol, J. M. **Orbital osteoma.** Rev. Oto-Neuro-Oft., 1934, v. 9, June, p. 187.

(See Amer. Jour. Ophth., 1934, v. 17, May, p. 468.)

Stieren, E. **Sarcoma of the uveal tract following trauma.** Jour. Amer. Med. Assoc., 1934, v. 103, Aug. 4, p. 311.

A man aged fifty-eight years received a lacerating injury of the conjunctiva of the globe which healed promptly. Nine years later a melanosis was found to have developed in the choroid in the region of the earlier injury. The six conditions stipulated by Segond were present, and the author has no hesitancy in ascribing the malignant growth in the choroid to the external injury of the eye. (Four figures, discussion.) George H. Stine.

Sykes, E. M. **Neurofibroma of the orbit in Recklinghausen's disease.** Texas State Jour. of Med., 1933, v. 29, Nov., p. 447.

A review of the history and literature of neurofibromatosis is given and the characteristic microscopic features of neurofibromata are outlined. A case of neurofibroma of the orbit is reported in a patient with multiple cutaneous fibromata. Edna M. Reynolds.

Van der Straeten and Maldague. **Four observations of sympathoma of the suprarenal capsule with ocular symptoms.** Bull. Soc. Franç. d'Opht., 1933, 46th year, pp. 410-431; also Bull. Soc. Belge d'Opht., 1934, no. 67, p. 118. (See Amer. Jour. Ophth., 1933, v. 16, Dec., p. 1141.)

→ Vassiliadis, H. **Cancer of the eyeball and its treatment.** Arch. d'Opht., 1934, v. 51, June, p. 348.

Cancer of the superficial portions of the eye such as the lids and conjunctiva is best treated by radium or x-ray. Malignant growths within the globe or orbit offer the best opportunity for cure with surgical intervention preceded and followed by intelligent radiotherapy. A detailed report of the results of treatment of thirty-seven cases of tumor of the globe is given. M. F. Weymann.

→ Vele, M. **Tumors of the lid.** Boll. d'Ocul., 1933, v. 12, Aug., pp. 788-831.

Clinical histories and histologic findings are given for ten tumors of the eyelid, three of which, of epithelial origin, affected the meibomian glands or the lid margin. Among tumors of connective tissue origin are reported different varieties of fibroma and sarcoma. The author discusses the indications and the results of surgical, radium, x-ray, jequirity, and carbon-dioxide snow treatment. The age of the patients, four of whom were male, varied from two months to seventy years. (Bibliography, twenty-two figures.) M. Lombardo.

→ Vos, T. A. **Papilloma of the tear sac.** Klin. M. f. Augenh., 1934, v. 93, May, p. 658.

In a woman of seventy-seven years with a mass in the region of the tear sac which was not entirely compressible, histologic preparation from the excised tissue revealed an unequivocal papilloma. This is the only one ever seen in the Gronigen clinic, and Kuhnt believed the tumor one of the greatest of rarities.

F. H. Haessler.

## 16 INJURIES

Bietti, Giambattista. **Further contributions to our knowledge of the retrolenticular pigment ring and its development.** Klin. M. f. Augenh., 1934, v. 93, July, p. 54.

A description of two cases of annular pigmentation of the posterior lens capsule is presented. In one the ring was complete except for a few short interruptions; in the other the line was a semicircle. One followed an Elliot trephining and the other multiple episcleral cauterization with carbon dioxide snow for retinal detachment. In one case no pigment whatever was formed on the posterior corneal surface and in the other only a few granules. In all other published cases a Krukenberg spindle or diffuse postcorneal pigmentation was noted. Rapid disappearance of the rings could also be observed.

Apparently the aqueous not only reabsorbs the pigment but must carry a large supply in order to keep the ring developed. The distribution is probably determined by the space between lens

and vitreous. It is clear that during disintegration of uveal cells pigment may become deposited on the lens surface, the corneal surface, or both.

F. H. Haessler.

Brindley, B. I. **Melanosarcoma of iris and ciliary body; report of a case.** *Wisconsin Med. Jour.*, 1934, v. 33, May, p. 359.

In a woman of sixty-six years a brownish-black thickening of the iris, accompanied by an increase in intraocular pressure, led to enucleation of the eye, and the clinical diagnosis of melanoma was confirmed. Microscopic examination revealed considerable involvement of the ciliary body.

John C. Long.

Davis, W. T., and Morrison, F. McC. **Cilium implanted in the cornea.** *Amer. Jour. Ophthalm.*, 1934, v. 17, Aug., p. 746.

Dollfus, Marc-Adrien, and Halbron, Pierre. **Contribution to study of the prognosis of penetrating wounds of the globe. (Statistical studies.)** *Arch. d'Opht.*, 1934, v. 51, June, p. 365.

This article does not lend itself to abstraction since it is a compilation of figures concerning the etiology, prognosis, and treatment in 394 patients seen at the Hôtel-Dieu who suffered penetrating wounds of the globe. Of forty-four intraocular magnetic foreign bodies removed by the anterior route and fifteen by the posterior route a comparison of ultimate results showed very little difference. Only 23.3 percent of those injured recovered useful vision, while more than one-half lost the entire vision of the injured eye. M. F. Weymann.

Gill, W. D. **Fractures of the facial bones with special reference to involvement of the paranasal sinuses and orbits.** *South. Med. Jour.*, 1934, March, p. 197.

The various types of fracture of the facial bones with their complications are discussed. These bones reunite quickly so that prompt reduction is necessary. The serrated edges of some of the fractures make fixation simple but wiring is often required. Types of treat-

ment suitable to individual fractures are discussed.

John C. Long.

Hesky, M. **Clinical contribution to ocular changes from intraocular aluminum splinters.** *Boll. d'Ocul.*, 1933, v. 12, Aug., pp. 832-857.

Describing a case of penetrating wound by aluminum splinters one of which was seen freely moving in the anterior chamber, and after a description of the changes in the tissues of the eye from different metals, the author concludes that aluminum inside of the eye undergoes chemical changes which in turn have a toxic effect on the different ocular structures. (Bibliography.)

M. Lombardo.

Hudelo, A., and Hermann. **Epithelial invasion of the anterior chamber.** *Arch. d'Opht.*, 1934, v. 51, June, p. 356.

The case reports of two patients with epithelialization of the anterior chamber following a perforating wound of the eye and a cataract operation, respectively, are given with excellent photomicrographs of the sectioned eyes after enucleation. It is particularly noted that epithelial ingrowth occurs after a wound in which there is incarceration of a foreign substance. In the first case described secondary glaucoma did not occur, but, without serial sections, there is no proof that epithelialization of the entire angle occurred.

M. F. Weymann.

Jess, Adolf. **Extraction of roentgen cataract. Cystin reaction in the lens in roentgen cataract.** *Zeit. f. Augenh.*, 1934, v. 83, June, p. 261.

Four years after radiation the beginnings of lenticular opacity were observed bilaterally. The opacities were posterior shells, most intense at the pole. One lens was extracted six years after radiation, when the entire center was opaque. In frozen sections the parts corresponding to the posterior shell and the central mass of the lens remained colorless, while the periphery elsewhere stained an intense red when treated with sodium nitroprusside and ammonia. Since Jess has shown that the cystin reaction is associated chiefly



with beta crystalline, only slightly with alpha crystalline, and not at all with albuminoid, one may conclude that in roentgen as well as senile cataract the opacity develops with loss of the soluble crystalline. Cystein, which is of particular importance in the inner respiration of the tissue, is present only in the utmost periphery. (It is interesting to note that the roentgen rays which caused the lenticular opacity inhibited the growth of a slowly growing hypophyseal tumor for which they were given.)

F. H. Haessler.

Ohm, J. **The demonstration of metallic foreign bodies by means of thermionic amplifier tubes.** Zeit. f. Augenh., 1934, v. 83, June, p. 287.

Comberg and Hata have recently used amplifier tubes in the diagnosis of intraocular foreign bodies. Each used a coil as finder, and as an indicator one used an ampere meter and the other a loud speaker. Ohm points out that he called attention to the principle in 1929.

F. H. Haessler.

Salvati. **A foreign body (a piece of crayon) implanted in the orbit for six months.** Bull. Ophth. Soc. of Egypt, 1933, v. 26, p. 167.

A child with unilateral exophthalmos had fallen on a pointed crayon six months previously. There was a small fistula at the site of injury to the upper lid. The case is reported because of absence of inflammation, which the author ascribes to the fact that the foreign body was encapsulated in the orbital fat and was not in contact with the vascular tissues or the orbital walls.

Edna M. Reynolds.

Walker, S. J. **Bacillus welchii panophthalmitis.** Jour. Amer. Med. Assoc., 1934, v. 102, May 12, p. 1561.

An automobile mechanic developed panophthalmitis following perforation of the globe by a piece of steel. Gas bubbles were seen in the anterior chamber twenty-four hours after the injury, and pus taken from the eye was positive for *Bacillus welchii*. Evisceration and drainage, and massive doses of B. tetani and B. welchii serum were followed by uneventful recovery in twelve days.

The author points out that, although rarely, intraocular steel is a potential carrier of *B. welchii*. This case is only the second one reported in the United States. Early diagnosis is of prime importance. *B. welchii* panophthalmitis apparently has not the grave prognosis that this infection has in other parts of the body, possibly because of the fact that the infection is limited to nonmuscular tissue.

George H. Stine.

#### 17. SYSTEMIC DISEASES AND PARASITES

Abreu, Jr. **Tuberculosis of the eye.** Annaes de Oculistica do Rio de Janeiro, 1933, v. 5, no. 2, pp. 9-65.

This is a fifty-seven page thesis in Portuguese, which was presented to the Madrid International Ophthalmologic Congress, 1933. The author praises the effect of a proprietary preparation named "gadusan" which contains cod-liver oil.

W. H. Crisp.

Accard', V. **The eye and the endocrine glands.** Rassegna Ital. d'Ottal., 1934, v. 3, March-April, p. 279.

This paper is in substance a lecture delivered to the faculty and students of the University of Modena. It gives a good review of the generally known relationships between disturbances of the endocrine glands and the eye. It is not adapted to review.

Eugene M. Blake.

Berens, C., Connolly, P. T., and Chapman, G. H. **Focal infection in diseases of the eye. 1. Report of certain laboratory examinations.** Brit. Jour. Ophth., 1934, v. 18, Aug., p. 463.

This study concerns itself with, serologic methods, bacteriologic methods, general considerations of certain foci, and clinical diagnosis. The authors believe that the presence of a high agglutinin titer to an autogenous strain of streptococci is strong presumptive evidence that the strain is related to a focus of infection. But in a number of instances inagglutinable or weakly agglutinable organisms were undoubtedly of focal origin. Simultaneous use of a number of different serobacteriologic reactions has given information as to the identity and probable location of or-

ganisms thought to be responsible for lesions of the eye. These reactions are of decided value to the ophthalmologist in studying diseases of the eye which are possibly due to focal infection. The tests are of value in determining the process of treatment.

D. F. Harbridge.

Bothman, Louis. **Endocrines in ophthalmology.** Illinois Med. Jour., 1934, v. 65, March, p. 226.

The author briefly discusses the numerous ocular manifestations of abnormal function of the thyroid, thymus, parathyroids, pancreas, gonads, adrenals, and hypophysis. The influence of the endocrines in migraine and in abnormal intraocular pressure is mentioned.

John C. Long.

Mazzola, V. **Ocular disturbances of female genital origin.** Lettura Oft., 1934, v. 11, Feb., p. 53.

Numerous bibliographic notes on the subject are given. The author carried out a systematic study of visual fields, ocular tension, accommodative power, and chromatic sense in puberty, menstruation, pregnancy, and the period of lactation. He concludes that during menstruation, in a small percentage of cases, concentric contraction for white and colors occurs, and sometimes a very slight rise in tension, especially where the menstrual flow is heavy. The accommodative power in forty percent of the cases diminished one to three diopeters. In pregnancy there was constriction of fields in the form of bitemporal hemianopsia, diminished tension, and accommodative power. In puberty and during lactation no change of note occurred. (Tables, bibliography.)

F. M. Crage.

Motegi, A., Kan, T., Ko, S., and Syu, S. **Ophthalmologic observations in one hundred cases of malaria.** Klin. M. f. Augenh., 1934, v. 92, June, p. 797.

In one hundred consecutive patients with malaria, forty-five were found to have lesions of the eye. The lesions included trachoma, pterygium, symblepharon, macula corneae, iris, synechia, punctate equatorial cataract, vitreous opacity, retinitis proliferans, myopia,

and persistent hyaloid artery. Visual acuity was no less than in any other group, nor was near point of accommodation, peripheral field, or blind spot. Greyish discoloration of the retina about the disc was commonly observed. Punctate hemorrhages were not uncommon. The bulbar conjunctiva was yellow. In ten of the one hundred cases of malaria, the discoloration disappeared with therapy.

F. H. Haessler.

Ortiz, J.-M.V. **A new clinical form of the nasal nerve syndrome.** Ann. d'Ocul., 1934, v. 171, June, pp. 479-484; also Rev. de Ophth. de São Paulo, 1934, v. 3, June, p. 230.

To the clinical types of this condition already pointed out by Charlin is added this new one. The patient, a twenty-seven-year-old woman, had violent neuralgia in the left orbital and frontal region, with photophobia and epiphora, the cause of which had not been found. The eyeball was tender, the bulbar conjunctiva red, and there was a nasal discharge, all on the same side. The symptoms were relieved by spraying the anterior part of the left nasal fossa with cocaine and adrenalin, and this treatment was repeated for five days, with the understanding that if the symptoms returned an irritating nasal spine would be removed. The proof of the diagnosis in these cases lies in the response to treatment.

H. Rommel Hildreth.

Riehm, W. **A contribution to the classification of conceptions of allergy. The relations between anaphylaxis and immunity.** Klin. M. f. Augenh., 1934, v. 92, June, p. 721.

Workers in immunity and allergy in many instances use the same words to designate different concepts, and great confusion exists. Riehm outlines his conceptions of the entire process of immunity and allergy and defines all the terms he uses. He suggests that those who do not wish to follow him are at least obliged to formulate their own definition precisely. Immunity denotes an injury to invading organisms by antibodies; anaphylaxis, a similar injury to body cells.

F. H. Haessler.

Santonastaso, A. **The relation of cholesterinemia and calcemia in degenerative ocular infections.** *Ann. di Ottal.*, 1934, v. 62, June, p. 433.

Noting the frequency with which fatty degeneration in the ocular tissues is associated with calcium deposits, the author made special study of eight cases including xanthomatosis, synchysis scintillans, xanthelasma, gerontoxon, and cholesterin crystals in the crystalline lens and the anterior chamber, with a view to determine whether the cholesterinemia or the calcemia was in excess. He considers the local conditions favoring the fatty or calcic deposits to be dependent on vascular retardation due to inflammatory obstruction and a reciprocal interaction between the lipoids and the electrolytes. He also thinks that this is influenced by the effect of certain hormones on the sympathetic nervous system. Park Lewis.

Schmidt, Karl. **Clinical investigation of the relationship between lesions of the teeth and eyes.** *Klin. M. f. Augenh.*, 1934, v. 93, July, p. 19.

In thirty-nine eye lesions the findings of dental x-rays are tabulated. In most of the cases teeth with root granulomata were extracted. In two the lesion healed, in one there was improvement. The author reminds the reader that mere finding of a dental root lesion does not demonstrate a causal relationship to the eye lesion. It is very possible that a person with an inactive tuberculosis may acquire an iritis from an infection at the apex of a dental root. Extraction of a tooth with the incidental hemorrhage and production of a large wound with consecutive breaking down of tissue may bring about a nonspecific protein therapy. F. H. Haessler.

Spadavecchia, V. **Epidemic encephalitis and its ocular manifestations.** *Ann. di Ottal.*, 1934, v. 62, May, p. 412, and June, p. 452.

The various forms in which this disease manifests itself are considered. In certain instances the ophthalmic symptoms are the only apparent ones and may serve to differentiate this from a hysteric or neurasthenic condition.

Eight cases were studied in detail. In four the ocular muscles were affected; in the remaining four there were otic involvements. The author formulates the hypothesis that the smaller encephalic vessels, especially vulnerable to the infecting material, are the initial seat of the lesion, the virus with its toxins being carried into the general circulation to create centers of functional disturbance. In this way he accounts for the variety and the transitoriness of many of the symptoms. (Bibliography.) Park Lewis.

Viallefont, H., and Lafon, R. **The diencephalomesencephalic origin of ocular signs in Basedow's disease.** *Ann. d'Ocul.*, 1934, v. 171, June, pp. 495-507.

The ocular signs found in exophthalmic goiter are especially motor disorders that can be interpreted as manifestations of disturbances in the central nervous system in the diencephalomesencephalic region. The motor disorders are asynergies, hypertonies, and partial paralyses. The question naturally arises, is Basedow's disease primarily a nerve disease or does the abnormal thyroid gland secretion give rise to disturbed nerve function? Clinically four groups may be classified: (1) Basedow's disease appearing during or following a disease of the nervous system; (2) neurologic affections accompanied by ocular signs of Basedow's disease; (3) Basedow's disease accompanied by neurologic manifestations; (4) association of neurologic signs with the notably ocular phenomena of the Basedow type. H. Rommel Hildreth.

#### 18. HYGIENE, SOCIOLOGY, EDUCATION, AND HISTORY

Barrett, James. **Causes of blindness.** *Med. Jour. Australia*, 1933, v. 2, 20th yr., Dec. 30, p. 872.

An analysis of the causes of blindness in 226 patients seeking admission to the Royal Victorian Institute for the Blind from 1923 to 1933 is presented. Venereal disease is responsible for one third of the total number of cases of blindness. Myopia is a major cause of blindness, accounting for 13.5 percent. Comparison of the cases from 1923 to 1933 with



those prior to 1923 shows definite decrease in ophthalmia neonatorum and trachoma but an increase in myopia and retinitis pigmentosa.

Edna M. Reynolds.

Chance, Burton. **A view into the ophthalmology of Galen.** Amer. Jour. Ophth., 1934, v. 17, Aug., pp. 718-721.

**General assembly of the International Association for the Prevention of Blindness and the International Organization against Trachoma.** (Proceedings of the meeting of the fourteenth of May, 1934.) Arch. d'Opht., 1934, v. 51, June, p. 379.

The proceedings of this meeting, consisting of papers by de Lapersonne, Park Lewis, Émile de Grosz, A. F. MacCallan, Issa Hamdi El Mazni Bey, Luigi Maggiore, Lasnet, Hermant, F. Wibaut, Cuénod, and V. Morax, appear in their entirety in this issue.

M. F. Weymann.

MacCallan, A. F. **Spanish-Arabic ophthalmology.** Brit. Jour. Ophth., 1934, v. 18, Aug., p. 460.

This is from a twelfth century Spanish-Arabic author, Mohammad ibn Quassoum ibn Aslam al-Ghafiqi. A large part of the manuscript is concerned with general medicine and only the sixth book or chapter is devoted to ophthalmology. Much of this was drawn from the work of Ali ben 'Isa of Bagdad about 1000 B.C. It includes references to the cataract operation,

with an excellent description of a couching operation. Also described are four kinds of trachoma, lacrimal abscess, collyria, and ointments.

D. F. Harbridge.

Pak, C., and Pillat, A. **Chinese eye drugs.** Chinese Med. Jour., 1934, v. 48, Feb., p. 101.

Native prescriptions for treatment of eye diseases are popular in China. Severe inflammations and corneal opacities have been frequently observed following the use of these preparations. Ten popular brands of eye drugs were examined. Most contained zinc and calcium carbonates, calcium oxide, camphor, and inert material. Some contained bat and bird feces. In rabbits all produced conjunctival irritation and some produced corneal opacity. The authors point out the urgent necessity for strict control of native eye drugs.

John C. Long.

Rohrschneider, Wilhelm. **The distribution of trachoma in Germany.** Zeit. f. Augenh., 1934, v. 83, June, p. 263.

An extensive statistical study made clearer by the help of maps is presented. It is obvious that the susceptibility of the harvester who comes in from contiguous countries as contrasted with the relative immunity of the stable agrarian population is not an inherited characteristic of race but rather the result of inadequate personal hygiene.

F. H. Haessler.

## NEWS ITEMS

News items should be sent to the Editor by the twelfth of the month.

### Deaths

Dr. Charles Victor Roman, Nashville, Tenn., aged 70 years, died August 23rd, of cerebral hemorrhage.

Dr. Christian Schaeffer, Columbus, Ohio, 64 years, died August 12th, of carcinoma.

Dr. Jay Clarence Knipe, Philadelphia, aged 65 years, died September 2nd, of coronary thrombosis.

### Miscellaneous

The Guerrant Mission Clinic and Hospital of Winchester, Kentucky, is to have added to its staff an Eye, Ear, Nose and Throat surgeon. The present equipment for this clinic

is inadequate and with no Church, State or County organization backing the work the clinic is dependent on friends. Eye, ear, nose and throat instruments and equipment and especially a slitlamp are desired. The Clinic serves the Kentucky mountain region.

A Cultural and Service Club for the Blind of St. Louis was organized in January 1934. The objectives of this club are education, entertainment, recreation and service. All officers except the secretary-treasurer are blind.

The University of Buffalo Gold Medal is awarded annually to the author of a work on

an ophthalmic subject. Details may be had by addressing Dr. H. W. Cowper, 543 Franklin street, Buffalo, New York.

### Societies

The Washington, D.C., Ophthalmic Society meets at the Episcopal Eye and Ear Hospital, 1147 Fifteenth street on the first Thursday in November, January, March and May at eight p.m. The officers are as follows: president, Dr. William Thornwall Davis; vice-president, Dr. Leroy Hyde; secretary-treasurer, Dr. James N. Greear.

Professor Dr. Hans Lauber of the University of Warsaw, Poland, gave a course of four lectures before the Washington Ophthalmological Society, September 29th to October 2nd, 1934, which were valuable and stimulating. Among the out of town men who journeyed to Washington to hear Professor Lauber were Dr. C. A. Clapp of Baltimore and Dr. H. C. Neblett of Charlotte, North Carolina.

Professor Lauber also lectured before the Medical Society of the District of Columbia, which was of particular interest because he lectured upon and demonstrated an instrument, which he and his assistant, Dr. Cernski, have perfected in the laboratory at Warsaw, by which the delicate differences in intracranial tension can be measured by measuring the effect on the retinal vessels of pressure on the globe.

The Eye Section of the Philadelphia County Medical Society has changed the date of its scientific meetings from the second Tuesday of each month to the first Thursday, October to May inclusive.

On January 19 to 25, 1935, the Primeira Reunião Brasileira de Ophthalmologia and other medical societies in Brazil will hold a national congress of ophthalmology in the city of São Paulo. Scientific contributions from any country are welcomed, and will be published in the transactions of the congress, twenty-five separate copies of each article being furnished the author without charge.

The Research Study Club of Los Angeles will present its fourth annual mid-winter clinical course from January 21 to February 1, 1935, in Los Angeles. The guest lecturers in ophthalmology will be Dr. Webb Weeks

of New York City who will give a course in operative surgery on the cadaver, and Dr. Harry Gradle of Chicago who will discuss the subject of glaucoma, uveitis, and the evaluation of recent advances in ophthalmology. The guest lecturers in oto-laryngology will be Dr. George Portmann of Bordeaux, France, and Dr. John Barnhill of Miami, Florida. As usual the ophthalmological subjects will be given in the forenoon while the course in oto-laryngology will occupy the afternoon. The courses in dissection and cadaver surgery will be given in conjunction with the University of Southern California Medical School. The fee for the entire course will be fifty (\$50.00) dollars. For further information and a detailed program of the course address Dr. Don Dryer, 2007 Wilshire Blvd., Los Angeles.

The International Medical Assembly and Interstate Postgraduate Medical Association of North America will meet in Philadelphia, November 5-9, 1934, inclusive. The hosts will be The Eastern Postgraduate Medical Association, The Medical Society of the State of Pennsylvania, and The Philadelphia County Medical Society.

The Annual Conference of the National Society for the Prevention of Blindness will be held in New York City, December 6-8, it is announced by Lewis H. Carris, Managing Director.

Dr. Edward Jackson of Denver, Colorado, will deliver the principal address on the subject, "A Wide Basis for Blindness Prevention." Dr. Jackson was the first recipient, in 1925, of the Leslie Dana Gold Medal which is awarded annually for outstanding achievements in the prevention of blindness and conservation of vision.

Among the topics that will come up for discussion at the Conference will be: the causes of blindness; sight-saving classes for children with seriously defective vision; prevention of eye accidents; and prevention of prenatal infections which may cause blindness.

### Personals

Dr. William H. Wilmer has returned to Washington and will resume his private practice in his office there.

Professor Bielschowsky arrived recently in this country. He is to be associated with the Department of Physiology at Dartmouth College.